INTERNATIONAL ABSTRACTS OF SURGERY

VOLUME 93 AUGUST, 1951 NUMBER 2

COLLECTIVE REVIEW

AMINO ACID MIXTURES AS PARENTERAL PROTEIN FOOD

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THE present review deals with the literature on the use of amino acid mixtures as parenteral protein food published during the years 1948 through June, 1950. The work before 1948 has already been described (27, 28, 29).

The highlights of the period under review were: the work of Rose on the requirements of the human adult for amino acids, the progress made in the development of fat emulsions suitable for intravenous administration, and in the use of alcohol (thereby supplying caloric needs during parenteral nutrition), the development of an amino acid preparation which can be administered at a very rapid rate, and, finally, the information obtained pertaining to the urinary excretion of parenterally administered amino acids and peptides.

TERMINOLOGY OF PROTEIN HYDROLYSATES AND AMINO ACID MIXTURES

The Council on Pharmacy and Chemistry of the American Medical Association has published a report (60), "Protein and Amino Acid Preparations," in 1948. The report consisted of a descriptive monograph regarding the action, uses, and dosage of these preparations. The Council required the preparations to be clearly designated to indicate the source of protein (casein or lactalbumin in the case of pure proteins, or blood or liver in the case of mixed proteins), as well as the method of hydrolysis (acid, enzymatic), and the nature of modification in amino acid content, e.g., removal of amino acids such as aspartic acid and glutamic acid, or the addition of essential amino acids such as tryptophan which are either destroyed during hydrolysis or are required in larger quantities. The parenteral solutions should be clearly marked to show the concentration of protein hydrolysate and glucose. The Council considers as acceptable for nutritional purposes only those mixtures that provide adequate amounts of each of the essential amino acids. For the present, the Council restricts acceptance to hydrolysates of pure proteins or good sources of protein in which more than 50 per cent of the total nitrogen is in the form of alpha amino acid nitrogen, this minimum degree of hydrolysis being considered essential to reduce antigenicity. The Council requires also adequate rat growth studies to demonstrate nutritive value and clinical evidence to demonstrate freedom from antigenic, pyrogenic, and toxic properties.

Varieties of amino acid mixtures. The various amino acid mixtures and protein hydrolysates employed for intravenous administration have been adequately described by Elman (29) elsewhere. Since then, a number of other preparations have been used by different workers and the products accepted by the Council on Chemistry and Pharmacy of the American Medical Association have been described in the Journal of the American Medical Association from time to time and in the

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TABLE I.—COMPOSITION OF VARIOUS AMINO ACID MIXTURES[1]

(Calculated as per cent of dry solids)

	Amigen[a]	Merck amino acids[b]	Parenamine[c]	Aminosol[d]	Travamin[e]
Total Nitrogen	12.0	13.3	13.7	13.4	12.0
Hydrolysis (Amino N as % of potential amino N)	75	100	93	69	65
Ash	5.5	1.0			
Arginine	3.2	2.5	3.2	4.8	3.8
Histidine	1.9	4.2	2.0	2.0	2.1
Isoleucine	4.9	8.0	4.5	3.8	3.0
Leucine	9.1	16.5	6.0	5.6	7.5
Lysine	5.1	9.4	5.8	7.0	6.8
Methionine[2]	2.6	4.0	3.7	2.8	1.1
			(0.75)	(0.50)	
Phenylalanine	3.9	5.3	2.8	3.0	3.2
Threonine	2.9	1.9	2.3	5.2	5.3
Tryptophan[2]	1.3	0.9	1.3	0.9	1.0
		(0.9)	(0.6)		
Valine	5.3	7.0	4.7	4.0	5.8
Glutamic acid	17.1	1.5		10.6	10.9
Tyrosine	4.6[3]	0.3	1.4	2.6	0.9
Glycine	0.4	23.0		5.6	
Aspartic acid	4.7	0.2		5.2	8.1
Proline	6.2			5.8	
Serine	4.9			7.0	
Alanine	4.2			3.8	
Hydroxyproline	1.5				
Cystine	0.3			2.4	2.1
Chlorine	1.5		0.17	Trace	
Sodium	1.5		0.50	0.2–0.4	
Phosphorus	0.9			0.01	
Sulfur	0.6			0.33	
Calcium	0.3			0.05	
Potassium	0.2			0.3	
Magnesium	0.05			0.01–0.02	
Iron	0.01			0.0008	
Copper	0.001			0.00002	
pH of solution as prepared for parenteral use	6.5	5.5–7.5	5.5	5.0–5.5	5.75

[1]The data refer to the amino acid content after complete hydrolysis in the case of products containing polypeptides. The source of the data in the case of each product is as follows:

[a]Amigen—protein hydrolysate for parenteral use. Handbook for Physicians. Mead Johnson and Co., Evansville, Indiana.

[b]Merck amino acids—data on the average composition supplied by the manufacturers, Merck & Co., Rahway, New Jersey.

[c]Parenamine—calculated from data contained in technical literature supplied by the manufacturer, Winthrop-Stearns Co., Detroit, Michigan.

[d]Aminosol—data supplied by the manufacturers, Abbott Laboratories, Chicago, Illinois.

[e]Travamin—data supplied by the manufacturer, Baxter Laboratories, Morton Grove, Illinois.

[2]The figures in parentheses in some products refer to D-forms which have been added.

[3]Most of the tyrosine in this product is removed by fractional crystallization.

publication "New and Nonofficial Remedies (NNR)," also published by the American Medical Association. It is not the purpose here to describe all the products individually, but to deal with a few of them which have been studied extensively and which are typical from the point of view of their composition. These fall into four distinct categories.

1. Enzymatic hydrolysates. Amigen® and travamin® are the best known of this type. They are made by digesting casein and bovine plasma proteins, respectively, with pancreatic enzymes, and they contain free amino acids and a small amount of peptides.

2. Partial acid hydrolysates. Aminosol®[1] (Abbott) is the best known of this type. Aminosol is prepared by partial acid hydrolysis of purified fibrin and contains both amino acids and peptides. A part of the tryptophan is destroyed during the acid hydrolysis.

3. Complete acid hydrolysates. Parenamine® is a representative of this type. It is obtained by the almost complete acid hydrolysis of casein. It contains free amino acids and a very little amount of peptides. During the acid hydrolysis all the tryptophan is destroyed and therefore the hydrolysate is fortified with DL-tryptophan.

4. Fractionated and fortified complete acid hydrolysate. This type is represented by Merck's "10 per cent amino acids solution," and elamine®. These preparations are derived from a complete acid hydrolysate of casein and are therefore free of peptides. The amino acids in the hydrolysate are fractionated by solvent extraction, and some of the fractions are recombined to give a mixture rich in essential amino acids and reduced amounts of the dicarboxylic (aspartic and glutamic) amino acids. Merck's 10 per cent amino acids solution is supplemented with the essential amino acids, DL-methionine and DL-tryptophan and the nonessential amino acid glycine. The practically quantitative removal of aspartic and glutamic acids is intended to reduce the unpleasant reactions of nausea and vomiting caused by rapid rates of injection. The addition of glycine (about 22 per cent of the total amino acids) is believed to improve the patient's tolerance to intravenous infusions of the amino acids mixture. The experience of many workers (referred to later) has shown that a preparation of this type has certain advan-

[1]Aminosol refers to the American product and not the Swedish preparation of the same name. The latter is a dialyzed enzymatic casein hydrolysate containing free amino acids and small peptides. Casydrol is the name of another enzymatic protein hydrolysate of British manufacture which has also been used clinically. These products are not included because sufficiently detailed data about them were not available to the author.

tages and that its development may represent a definite advance in parenteral nutrition.

The data on the composition of the six preparations mentioned above are presented in Table I for purposes of comparison.

AMINO ACID REQUIREMENTS OF MAN

A knowledge of the actual amino acid requirements of the human subject is essential for the development of suitable amino acid mixtures for clinical use, whether used orally or parenterally. Results of qualitative tests announced by Rose (65) in 1947 revealed that but eight amino acids given orally are required by adult man for the maintenance of nitrogen equilibrium even for long periods. The finding that arginine is not essential is not surprising since the adult rat and the adult dog can be maintained in nitrogen equilibrium without it. On the other hand, the observation that the adult man can do without histidine was quite unexpected since all the higher animals so far tested require this amino acid. Future investigations should demonstrate whether arginine and histidine are essential for the growing child and during disease, reproduction, and lactation.

Rose's classification of amino acids is shown in Table II.

TABLE II.—CLASSIFICATION OF AMINO ACIDS WITH RESPECT TO THEIR ROLE IN THE MAINTENANCE OF NITROGEN EQUILIBRIUM IN NORMAL ADULT MAN

Essential	Nonessential
Valine	Glycine
Leucine	Alanine
Isoleucine	Serine
Threonine	Cystine
Methionine	Tyrosine
Lysine	Aspartic Acid
Phenylalanine	Glutamic Acid
Tryptophan	Proline
	Hydroxyproline
	Histidine
	Arginine
	Citrulline

In 1949 Rose (66) summarized the progress made by his group in the determination of the quantitative amino acid requirements of the normal adult man for nitrogen equilibrium. The interesting observation was made that, while nitrogen balance could be established with whole casein at a caloric intake of 35 calories per kilogram of body weight per day, 45 calories per kilogram per day were required for nitrogen balance when a mixture of amino acids or an acid hydrolysate of casein plus L-tryptophan replaced casein. Replacement of casein by an enzymatic hydrolysate of casein led to a slight negative nitrogen balance on 35 calories per kilogram per day. No explanation was apparent for the higher caloric requirement for nitrogen equilibrium on diets containing hydrolyzed protein or amino acid mixtures. All further studies were carried out on healthy male graduate students on a safe allowance of 55 calories per kilogram per day.

General procedures, dietary regimens, and analytical methods employed throughout the series of studies were described by Rose, Johnson, and Haines (67). In demonstrating the minimum requirement of the organism for a given component, all amino acids were kept at constant amounts throughout the test except the one under investigation. The latter was progressively lowered and the nitrogen content of the ration was maintained by the addition of glycine, urea, or of both. After the minimum requirement for each amino acid had been determined, twice this amount was selected as the intake of the subjects in all subsequent experiments involving other amino acids. The minimum requirement was studied in a number of experimental subjects and the highest value in any subject was the minimum requirement adopted. Twice this amount was arbitrarily designated as the "recommended intake" for the purpose of the formulation of diets in practical nutrition. The results of the quantitative studies as summarized by Rose (66) are presented in Table III.

The results also showed that D and L-methionine are equally effective in the maintenance of nitrogen equilibrium in man, while D-phenylalanine is partially utilized and the D-modifications

TABLE III.—MINIMUM AND RECOMMENDED INTAKES FOR NORMAL MAN WHEN DIET FURNISHES SUFFICIENT NITROGEN FOR SYNTHESIS OF NONESSENTIALS (STRICTLY TENTATIVE VALUES).

Amino acid	Minimum daily requirements (gms.)	Recommended daily intake (gms.)	Subjects tested (number)
L-tryptophan	0.25	0.5	31*
L-phenylalanine	1.10	2.2	22
L-lysine	0.80	1.6	27
L-threonine	0.50	1.0	19
L-valine	0.80	1.6	23
L-methionine	1.10	2.2	13
L-leucine	1.10	2.2	8
L-isoleucine	0.70	1.4	8

*All of these subjects have been kept in balance on 0.3 gram or less.

of tryptophan, valine, leucine, isoleucine, threonine, and lysine appear to be inactive.

The role of nonessential amino acids. The tentative minimum requirements for nitrogen equilibrium in adult human subjects given in Table III are stated (66) to be applicable "when diet furnishes sufficient nitrogen for the synthesis of nonessentials." However, the experimental details so far published (66, 67) do not mention the inclusion of significant amounts of "non-essential amino acids." The experiments were set up in this way presumably because separate investigations are contemplated in the near future to ascertain the possible replacement of phenylalanine by tyrosine, and of methionine by cystine, choline, or by both. Whenever the concentration of an essential amino acid under test was reduced, it was replaced by glycine and urea, obviously in small amounts, in order to maintain a constant nitrogen intake. With the exception of the essential amino acid being tested, all other essential amino acids were included in the diets in quantities double the established minimum requirements. This excess amount of the essential amino acids can theoretically serve as a nitrogen source for the synthesis of the nonessential amino acids, although it has not been experimentally demonstrated that they can serve the needs as efficiently as the nonessential amino acids themselves. Racemic forms of valine, isoleucine, methionine, threonine, and phenylalanine were used in the diets. However, a major portion of the nitrogen of the D-amino acids is *not* available to the body since they are largely excreted in the urine unchanged (67, 75). Thus the surplus quantities of the essential amino acids and partially the D-methionine and D-phenylalanine could serve as the sources of nonessential amino acid nitrogen. This raises the question of imbalance between the essential amino acids, which was shown to cause growth retardation in rats (37) and even symptoms of toxicity (83). Future work should reveal whether the tentatively established minimum requirements of the essential amino acids for purposes of nitrogen balance in adults will be appreciably reduced or altered by the provision of a mixture of nonessential amino acids in the diet. Greater stimulation of growth by the inclusion of some of the nonessential amino acids in the diet was shown by Womack and Rose and Ramasarma *et al.* in studies on young rats and by Maddy and Elvehjem in young mice. There is need for more information on the amounts of the various nonessential amino acids that should be included in the diet, on the ratio of the essential to the nonessential amino acid nitrogen in the diet, and on the relative proportions of the different essential amino acids which would lead to the most efficient utilization of the total dietary nitrogen for purposes of growth in the young, for maintenance of the nitrogen balance and the body weight in the adult, and for repletion in the malnourished.

CALORIC INTAKE AND PROTEIN UTILIZATION

It is well known that in the absence of a sufficient intake of calories, especially in the form of carbohydrates, the tissue proteins, dietary proteins, or both, are broken down and oxidized in order to meet the caloric needs of the body. This leads to a negative nitrogen balance, an inefficient utilization of the dietary proteins, or both of these conditions. Much of the earlier work on this subject has been recently reviewed by Deuel, Jr.

During the period under review, many publications emphasized the importance of satisfying the caloric needs of the subjects in order to insure optimum utilization of the proteins and amino acid mixtures. There is much confusion and lack of general agreement on a desirable level of caloric intake in patients receiving nitrogenous nourishment in various forms and different routes. It is not possible to deal here with the increased caloric needs in different clinical conditions or with the disturbed nitrogen metabolism during disease states or following injury. Only some of the general aspects of the problem concerning metabolically normal or depleted adult subjects will be discussed.

Reference has already been made to the work of Rose (66) indicating an increased caloric need for the maintenance of nitrogen equilibrium when protein hydrolysates or amino acid mixtures are given orally as compared with the oral ingestion of intact proteins. The question of a similarly high caloric requirement with intravenous infusions of amino acid mixtures has not been studied extensively. However, the available clinical data place the requirement much lower than the 45 (or 55) calories per kilogram per day used by Rose. Indeed, it was possible to maintain positive nitrogen balances for short periods of time in dogs (28), in rats (10), and in human subjects (28) on low caloric intakes by giving relatively large amounts of protein. However, in terms of nitrogen utilization it is an inefficient procedure. In some of these studies it is obvious that some of the body stores of fat were utilized to supplement the low calories supplied by the ingested carbohydrate. Further, some of the discrepancies in the clinical literature may probably be due to variations in the amounts of body fat present and in the subject's capacity to utilize body fat under different clinical situa-

tions. For instance, Rose (66) reported that in occasional cases, particularly in tall and slender individuals who were underweight for their height, intakes higher than 55 calories per kilogram per day were found necessary when amino acids were fed orally, while generally about 45 calories per kilogram per day were sufficient in average subjects. High caloric requirements of about 50 calories per kilogram per day were also reported by Murlin *et al.* and by Bricker *et al.* in similar studies in human beings. While the fat stores of the body can be roughly estimated from the nutritional status of the individual, their utilization for the current caloric needs depends upon endocrine response, particularly that of the adrenal cortex (81). In the absence of any reliable means of assessing this capacity to utilize body fat for energy needs, it seems preferable (though not always practical) to provide adequate calories orally or parenterally.

In practical parenteral feeding, it is advisable for obvious reasons to give only as much intravenous fluid as is necessary. In one study (29) 2 liters a day were found to be a sufficient water intake under normal conditions. It is also advisable to limit the concentration of these fluids to about 10 per cent of solids, in order to prevent thrombosis which is likely with more hypertonic solutions. The question then arises as to what proportion of amino acids and glucose will lead to their most efficient utilization. Further, since a nitrogen-sparing action is exerted by carbohydrate and not by fat (18), it remains to be shown in what way additional calories derived from intravenous fat emulsions can improve the nitrogen utilization or the over-all nutrition when the minimum carbohydrate intake is already provided.

Benditt *et al.* (10) carried out careful studies on the interrelationship between protein intake and energy intake on the utilization of protein for tissue synthesis in standard protein-depleted rats. The results indicated that approximately 1,240 calories per square meter of body surface is the critical level below which the efficiency of utilization of the dietary protein is reduced, as judged by the gain in actual tissue protein per kilogram of body weight per day at a given level of protein intake. Increasing the caloric level above the critical level resulted in no increase in tissue protein, but increased the body fat and therefore the body weight. With an adequate caloric intake, increasing amounts of tissue protein were synthesized as the protein intake was increased. A reevaluation (11) of observations on men from the literature revealed that the energy needs of a normal man at bed rest were approximately the same as for the rat, about 1,500 calories per square meter of body surface per day, i.e., about 2,600 calories per day for an average-sized man having a body surface of 1.7 square meters. Since the therapeutic goal in the depleted patient is not a mere maintenance of nitrogen equilibrium but the fabrication of significant quantities of body protein, it was suggested that protein intake levels of from 2 to 4 grams per kilogram per day be used with an adequate caloric intake for the rapid rehabilitation of a depleted person.

Ellison and his coworkers studied the influence of caloric intake upon the fate of parenteral nitrogen (amigen) in protein-impoverished and emaciated individuals. Approximately 25 calories per kilogram of body weight per day were sufficient to maintain the body weight and nitrogen balance, but 35 calories per kilogram per day or more were required for a positive nitrogen balance and a gain in body weight. For this purpose they recommended the use of 3 liters of 15 per cent dextrose in 5 per cent amigen per day instead of the usual 5 or 10 per cent dextrose solutions. Such hypertonic solutions, however, are known to cause phlebitis which may limit the practical usefulness of this regimen. Mok *et al.* thought that the requirements can be met by 25 calories per kilogram or less and that the nitrogen balance cannot be improved by increasing the carbohydrate intake.

In a report entitled "Malnutrition and Starvation in Western Netherlands, September, 1944 to July, 1945" edited by Burger, Drummond, and Sandstead (48), the results of nitrogen balance studies on severely malnourished patients receiving milk proteins and oral protein hydrolysate are described. It was found that in general the nitrogen retention was proportional to the caloric intake, but not to the nitrogen intake. The nitrogen balance was negative when either the nitrogen intake was less than about 0.18 gram of nitrogen per kilogram, or the caloric intake was less than about 32 to 35 calories per kilogram. The caloric and nitrogen intakes being higher than these critical levels, the nitrogen retention showed a direct relation to the ratio of the nonprotein calories to the protein calories.

The nitrogen-sparing action of carbohydrate (and not fat) is well known (18). The recent work of Munro confirmed his earlier findings, which emphasize the importance of giving carbohydrate synchronously with the protein. Considerably more improvement in the nitrogen balance resulted when protein and carbohydrate were fed together to rats than when they were given 8 hours apart. No such changes were observed in similar experiments involving fat. Evidence was

obtained by Lockhart and Elman that the addition of hydrolyzed protein (amigen) or amino acids to the glucose solution which was given intravenously to metabolically normal human subjects increased the rate of utilization of glucose by the tissues. This was shown by a lower blood sugar level and less glycosuria when amino acids were present than when glucose alone was given. It was also observed that the maximum speed of injection of glucose into normal adult subjects without the production of glycosuria was approximately 0.5 gram per kilogram per hour.

In calculating the calories supplied by a given regimen, it has been the common practice to multiply the grams of protein ingested by 4 and to add it to the calories obtained from carbohydrate and fat. Benditt *et al.* (11) and Moore have questioned the rationale of this procedure in cases in which maximum tissue protein synthesis is desired and occurs, e.g., in growth and convalescence. They point out that at least the protein or amino acid equivalent to the net positive nitrogen balance has clearly been incorporated into the tissues and therefore cannot have yielded energy, and, indeed, has probably used up some energy in the synthetic process.

Intravenous fat emulsions. It was recognized early that the intravenous administration of suitable fat emulsions would be an efficient means of supplementing the caloric needs of patients and rapidly rehabilitating severely depleted persons unable to eat. McKibben, Ferry, and Stone showed in 1946 that fat emulsions given intravenously to the dog led to a gain in body weight, a change from negative to positive nitrogen balance, and to the deposition of body fat. More recently, studies (11, 12) using fat labeled with C^{14} have confirmed the utilization of fat in emulsions given intravenously to rats. When trilaurin containing carboxyl labeled lauric acid was administered intravenously, nearly 50 per cent of the injected C^{14} was recovered as carbon dioxide after 2 hours and 70 per cent after 4½ hours, demonstrating the ready availability of fats for energy purposes (34). When palmitic acid having the label on the sixth carbon atom was administered to rats, nearly 50 per cent of the C^{14} was recovered in the respiratory carbon dioxide after 24 hours (44, 85).

Much progress has been made in the methods of preparation and intravenous administration of fat emulsions. Geyer, Mann, and Stare (35) devised a simple turbidimetric method for the determination of the level of infused fat in the blood and for obtaining fat tolerance curves, which are expected to be of diagnostic value and a guide in the use of fat emulsions for intravenous nutrition.

Meng and Early have fed dogs, for 4 weeks exclusively by vein, a diet containing carbohydrate, amino acids (amigen), fat (a special fat emulsion furnishing 36 per cent of the caloric content), minerals, and vitamins. The dogs remained healthy and gained weight. Extensive physiologic tests before, and complete histologic study after, sacrifice failed to reveal any significant abnormalities attributable to the procedure. One dog given the same treatment with the sole omission of the fat lost 14 per cent of its initial weight, appeared apathetic and emaciated, and developed lesions suggestive of fatty acid deficiency.

The successful administration of fat emulsions combined with glucose and amino acid solutions to human subjects has been reported by several groups of workers (49, 73, 74). Mann *et al.* gave an emulsion containing 15 per cent coconut oil to man in amounts up to 600 milliliters per day without unfavorable reactions. However, the emulsions developed pyrogens, probably of nonbacterial origin, after about 4 weeks of storage. Shafiroff *et al.* (74) described a special apparatus for preparing, under sterile conditions, a combined fat (10 per cent) emulsion which remained stable for more than 2 years. This emulsion was infused intravenously into 76 human subjects without any toxic effects or late sequelae. Positive nitrogen balance was established in 22 surgical patients with this combined emulsion (73).

The usefulness and safety of the intravenous administration of fat seems to have been well established, and it may not be long before carefully standardized products will be generally available for clinical use.

Ethyl alcohol (5 per cent) has been administered intravenously by Rice (61, 62) to more than 800 surgical patients as a safe and effective supplement to glucose (5 per cent) for supplying calories and thereby establishing a strongly positive nitrogen balance with parenterally administered amino acids (5 per cent). Administration at the rate of 15 milliliters of alcohol per hour to the average-sized adult will not produce symptoms of intoxication but will cause the blood alcohol to rise slowly to 0.08 per cent and then level off. This level produces mild sedation and analgesia, thereby reducing the need for morphine.

THE NUTRITIVE VALUE OF AMINO ACID MIXTURES

During the period under review, much valuable information regarding the estimation of the nutritive value of protein hydrolysates and amino acid mixtures has accumulated.

Allison (2, 3) has written two excellent reviews pertaining to the biological evaluation of proteins

and the utilization of protein hydrolysates by normal and protein-depleted animals. Allison, Anderson, and Seeley (4) represented the relation between absorbed nitrogen (AN) and nitrogen balance (NB) by the formula:

$$NB = K(AN) — NE_0$$

in which NE_0 is the nitrogen excretion on a protein-free diet and K has been called "the nitrogen balance index with respect to absorbed nitrogen," a measure of the rate at which the protein stores of the body are being filled. The nitrogen balance index is a constant characteristic of any particular protein source when normal well-fed animals are employed for the determination of the index.

The nitrogen balance index is a function of the "biological value," as defined by Thomas and Mitchell, and is not equal to it. The index is 1 when all the absorbed nitrogen is utilized for protein synthesis. Thus, egg white and lactalbumin were found to have an index of 1. Inferior sources of protein have indexes of less than 1. Indexes higher than 1 are obtained only when the normal breakdown of body protein is spared, e.g., an index of 1.5 was obtained on feeding casein plus methionine, whereas the index for casein alone was 0.8.

Allison, Seeley, and Ferguson (6) determined the nitrogen balance indexes of four different protein hydrolysates using normal dogs as experimental animals and a slightly modified formula for the calculation of the indexes. They observed that the nitrogen balance indexes were higher when the hydrolysates were fed orally (0.8) than when given intravenously (0.6–0.67). The index was greater in the protein-depleted dog (0.82) than in the normal animal (0.67), which showed a more efficient utilization of the amino acids given intravenously to the depleted animal.

The work of Christensen and others on the urinary loss of peptides present in an intravenous infusion of a protein hydrolysate solution was discussed earlier (29). The nutritive value of a protein hydrolysate may be seriously reduced by the urinary wastage of critical amounts of essential amino acids in peptide form. Allison (5) and his coworkers studied the effect of the extent of enzymatic hydrolysis on the nutritive value of casein. For this purpose, they prepared (13) casein hydrolysates in which 18, 38, and 59 per cent of the amino acids were liberated by using trypsin and carboxypeptidase. Oral feeding of these hydrolysates showed that they were equal to casein in their nitrogen balance indexes in adult dogs (0.67–0.69, casein 0.68) and in their protein efficiencies in rats (2.2–2.6, casein 2.3).

When the 18, 40, and 60 per cent enzymatic hydrolysates were injected intravenously into 3 adult dogs, respectively, the nitrogen balance indexes (0.52 ± 0.08, 0.50 ± 0.08, and 0.57 ± 0.09, respectively) did not show any differences of statistical significance. Compared with the preinfusion levels, the urinary excretion of free amino acids increased only slightly, while the excretion of peptide nitrogen increased markedly. However, the degree of hydrolysis (whether 18, 40, or 60 per cent) did not affect the peptide excretion significantly.

The most common method of determining the nutritive value of a protein or protein hydrolysate in a dry condition is to incorporate it into a ration supplying all the other nutritional requirements and studying the growth of young rats on the ration. There is a serious difficulty in the application of this method of assaying the solutions of protein hydrolysates and amino acid mixtures manufactured for intravenous use, because the young rats do not drink enough of the solution. Friedman and Kline tried to dry two pancreatic hydrolysates of casein with and without glucose under a variety of experimental conditions. The resulting dry materials were assayed by the rat growth method. They reported that "in the presence of glucose the nutritive quality of protein hydrolysate solutions deteriorates," but they presented no experimental data to show deterioration of the solutions under normal conditions of storage. The dried preparations, however, did suffer extensive losses in biological value. The nutritive damage was greatest when the protein hydrolysate solution was dried together with glucose at elevated temperatures. The development and the intensity of the brown color were a rough index of the heat damage resulting from the reaction of some amino acids with glucose. These reaction products seem to be better utilized by microorganisms than by the rat. This raises the question of the validity of microbiological assay values for heat-damaged proteins as a means of assessing the nutritive value for animals.

Frost and Sandy (32) have developed a method for determining the amino acid adequacy of liquid protein hydrolysates which would not necessitate drying of the solutions. This is a modification of the "rat repletion" method used by Wissler *et al.* (91) for evaluating protein hydrolysates intended for oral use. The basis of these methods is the observation (30) that for tissue protein and body weight recovery the adult protein-depleted rat requires all of the nine amino acids essential for nitrogen balance of the normal adult rat, and that (80) during repletion, changes in the gross

weights of the rats directly paralleled the gains in carcass protein, which indicated that the former give a good indication of amino acid utilization for tissue protein synthesis. The rat repletion method is more rapid than the rat growth method, and seems to be well suited for the assaying of amino acid solutions because of the ability of the adult rats to consume large volumes of liquid nutrients.

Young adult male rats were placed on nonprotein diets for a period of 12 days, when the average weight loss was 24 per cent. The 5 per cent hydrolysates or amino acid solutions were offered in drinking tubes instead of the usual water and the protein-free diet was supplied separately ad lib. The weight recovery of these rats was compared over a 12 day period with that of similar rats receiving defatted whole egg. It was found that liquid hydrolysates and pure amino acid solutions of good nutritive composition were readily accepted and they produced weight recoveries approaching those produced by the addition of whole protein to the diet. Several applications of this method were described by Frost and Sandy (33), who observed that the sulphur amino acids contained in partial acid hydrolysates of casein are not efficiently utilized when taken orally by the rat.

Many workers reported that mixtures of pure amino acids and complete acid hydrolysates of protein supplemented with tryptophan were nutritionally far inferior to whole proteins. It was concluded, therefore, that whole proteins contain some unknown factors, presumably of the type of the peptide strepogenin, which are destroyed by acid hydrolysis. Silber and his coworkers (77) fed 2 adult dogs orally with a peptide-free mixture of amino acids (Merck's VUJN type) for 40 days, and intravenously for a further 24 days. Body weights, serum protein concentrations, and nitrogen balances were maintained, but no evidence of toxicity or deficiency was observed. Two 12 week old beagle pups were fed orally for 12 weeks with a diet containing the same amino acid mixture as the sole source of nitrogen. The average weight gain was 0.4 kilogram per week, while their litter mates on a casein diet gained 0.43 kilograms per week. Again there was no evidence of toxicity other than an initial transient nausea in the pups receiving the amino acid mixtures. It was concluded, therefore, that peptides are not essential for the growth or maintenance of dogs. A similar conclusion was reached by Frost and Sandy (32) in rat repletion studies, by Ramasarma *et al.* in rat growth studies, and by Maddy and Elvehjem in studies with young mice.

Hoffman *et al.* examined a lyophilized preparation obtained by complete acid hydrolysis of casein followed by the removal of a substantial portion of the glutamic and aspartic acids present by a special process and supplementation with tryptophan (Amino Acids—I.C., lyophilized, Interchemical). Reconstituted to a perfectly clear 10 per cent solution, it was well tolerated when given intravenously. A positive nitrogen balance was attained in 19 of the 20 patients with chronic protein deficiency who were studied. The nitrogen intake required for equilibrium varied from 42 to 350 milligrams per kilogram per day, the average being 120 milligrams with a standard deviation of 51 per cent. The preparation was considered to be nutritionally and clinically adequate.

The nutritive value of gelatin and plasma proteins. During recent years, especially prepared ossein gelatin has been developed as a plasma substitute and has proved to be remarkably free from toxic and antigenic properties. As a source of protein, however, it is seriously lacking in some of the essential amino acids and cannot, therefore, support growth or nitrogen balance. There is not much information in the literature on the metabolism of gelatin given intravenously and its value as a food supplement. Riegel and his coworkers made the somewhat unexpected observation that the replacement of half of the protein hydrolysate in the daily intravenous infusion by gelatin resulted in a better nitrogen balance in spite of the fact that about 43 per cent of the injected gelatin was excreted in the urine unchanged. The studies were made on 20 surgical patients for 5 days after major abdominal operations such as gastric resection. The patients received, intravenously, approximately 30 calories per kilogram per day and 0.3 gram of nitrogen as a protein hydrolysate (derived from fibrin and casein; but its name was not mentioned). In half of the patients 50 per cent of the nitrogen was replaced by gelatin (Knox P-20). Gelatin, in a practically unchanged and precipitable form, was excreted in the urine during the 5 day period of administration and also for 3 days after the administration was discontinued. The latter value was added to the nitrogen excretion for the purpose of calculating the nitrogen balance. There was considerable variation in the nitrogen balances in the different individuals in each group. The average daily nitrogen balance in the group receiving protein hydrolysate alone was —2.8 grams, while the average for the group receiving hydrolysate and gelatin was —0.2 gram. The difference may not be of high statistical significance, but it is to be noted that replacement of half of the adequate protein hydrolysate

by the incomplete protein (gelatin) did not result in a more negative nitrogen balance. No explanation for these results was established, but the possibility that part of the gelatin was stored in the body was mentioned and seems quite likely. The reviewer believes that the nitrogen balance technique is inadequate for a study of the utilization of macromolecules of gelatin, blood, and plasma proteins given parenterally as they may be retained in the body and excreted slowly with or without further breakdown into smaller (non-protein) aggregates. Other criteria should be employed to demonstrate that these proteins enter the metabolic pool and take part in the dynamic equilibrium of the body proteins.

Allen and others compared the effects of amigen and plasma given intravenously upon the plasma proteins and nitrogen balance in a patient who had undergone a radical mastectomy. The patient received 2.4 grams of nitrogen per day orally and was in an average negative nitrogen balance of 2.3 grams per day. For 8 days amigen (9 grams of nitrogen per day) was given intravenously and the patient was in an average positive nitrogen balance of 1.6 grams per day. During a subsequent 4 day period, plasma was given at the rate of 8.8 grams of nitrogen per day, and a positive nitrogen balance of 11.9 grams per day resulted. It was stated that "when comparable quantities of nitrogen were administered the nitrogen balance achieved during plasma administration was about six times greater than during Amigen therapy." However, an examination of the data reveals that the daily nitrogen intake during the amigen period was 13 grams, while it was 17.3 grams during the plasma period, the difference being due to changes in the oral food intake. The total circulating plasma proteins did not change during the amigen period, but increased from 163.2 grams to 237 grams by the end of the 4 day plasma period. The period following the plasma transfusion was not studied in this patient, but data were presented in another patient to show that during 28 days following 5 days of plasma transfusion, there was no "latent nitrogen loss." On the other hand, there was a marked increase in nitrogen excretion during the amigen administration. It was concluded, therefore, that "intravenous plasma appears to be utilized more efficiently than intravenous amigen as a means of correcting plasma protein deficiency both with respect to nitrogen balance and elevation of plasma proteins." However, the metabolic studies of Waterhouse *et al.* on patients receiving a large part of their nitrogen intake from human serum albumin administered intravenously showed the hazards attending such a procedure. In all these patients, proteinuria developed eventually, probably not due to renal damage but due to saturation with albumin.

Earlier studies demonstrated the nutritive value of human serum albumin administered in the intact form to human subjects orally or intravenously. Eckhardt and Davidson (24) have investigated the nutritive value of an acid hydrolysate of human serum albumin supplemented with L-tryptophan given intravenously to a slightly undernourished subject. The patient was in nitrogen equilibrium on a basal diet supplying 50 grams of protein per day. Supplementation of this diet by the daily intravenous administration of 70 grams of hydrolyzed albumin led to a sustained positive nitrogen balance of 6.2 grams daily. A similar amount of hydrolysate given as the sole source of nitrogen was able to maintain the patient in a slightly positive nitrogen balance (0.9 gram daily). The results indicate that the amino acids of human serum albumin are nutritionally adequate and that they are metabolized and excreted in a manner similar to that of other protein hydrolysates.

Regeneration of various tissue proteins. Allison (3) has reviewed recent work on the reduction in the protein stores in different organs of the body when the experimental animal is placed on a protein-free diet or is subjected to plasmapheresis, and the effect of various dietary proteins and amino acid mixtures on the rates of regeneration of these tissue proteins. The important finding that has come out of these investigations is that depletion does not lead to a uniform loss of protein from all the tissues so that the amino acid requirements of a depleted animal are not the same as those of a normal or a growing animal. Conversely, during repletion, proteins and amino acid mixtures having different amino acid patterns, produced varying rates of regeneration of a certain tissue protein, although the amount of nitrogen retained may be the same. A certain mixture of amino acids has been shown to cause one type of tissue to be built up at the expense of others. After further elucidation of these complex mechanisms, it should be possible to devise ideally suited amino acid mixtures for each clinical condition involving protein deficiency. Chow and his coworkers (14) studied the effect of retention of nitrogen in pancreatic digests of casein and lactalbumin fed orally on the regeneration of plasma proteins in protein-depleted dogs. While confirming and extending their earlier observations, they found that the lactalbumin hydrolysate stimulated the production of albumin but with a marked decrease in alpha globulins, while casein hydro-

lysate alone or supplemented with methionine favored the production of both albumin and globulin. Since the difference in plasma protein regeneration is not due to the amino acid composition of the two hydrolysates nor to the amount of nitrogen retained, it was suggested that there may be as yet unidentified factors present in proteins and their hydrolysates which play a role in plasma protein synthesis.

Oral versus parenteral administration. Alper *et al.* carried out long term experiments to compare the utilization of parenterally supplied enzymatic hydrolysates of casein with the utilization of the same hydrolysates given orally. Adult mongrel dogs were depleted of protein by feeding protein-free diets with and without the accompaniment of plasmapheresis. The dogs were repleted by parenteral infusion for 24 to 25 days, followed by a similar period of oral feeding of approximately the same amount of the hydrolysate. Although partial repletion was produced by the intravenous infusion, nearly twice as much nitrogen was retained following the oral feedings as after the parenteral feedings. It was also noted that the gain in protein per kilogram of body weight per calorie of intake when the hydrolysate was given orally was twice that when the hydrolysate was given parenterally to animals subjected to extensive depletion. These differences are far greater than those already described (6) in shorter periods of observation.

THE METABOLISM AND URINARY EXCRETION OF INFUSED AMINO ACIDS AND PEPTIDES

During the period under review, many interesting studies were made on the utilization and urinary excretion of amino acids and peptides when protein hydrolysates and amino acid mixtures were administered intravenously. The important findings of Christensen and others (reviewed earlier, 29) on the urinary wastage of more of the peptides than of amino acids in infusions of partial protein hydrolysates have been confirmed and extended (5, 20, 78, 80).

The work of Allison *et al.* (5) on the effect of varying degrees of hydrolysis on the nutritive value of casein when given intravenously to dogs has been discussed earlier in this review. When these enzymatic hydrolysates of casein in which 18, 40, and 60 per cent of the amino acids were liberated were injected into dogs, it was observed that there was only a slight increase in the urinary excretion of alpha-amino nitrogen. The excretion of the peptides, however, increased markedly with no apparent effect from the degree of hydrolysis. A surprising conclusion (8) drawn from their experimental data was that the action of carboxypeptidase in converting the "18 per cent hydrolysate to the 40 per cent hydrolysate" rendered the resulting peptides more than twice as liable to spillage, which indicated that some types of peptides, irrespective of their size, are poorly utilized.

Eckhardt and others (20) reported that 75 grams of a partial protein hydrolysate (amigen) given intravenously daily for 4 days as the sole source of nitrogen (with the rest of the intake supplied orally and following the infusion) were able to maintain body weight and nitrogen balance in a normal subject. The hydrolysate contains two-thirds of its total amino acids in free form and one-third in peptide form. While less than 5 per cent of the infused free alpha-amino nitrogen appeared in the urine, the peptide alpha-amino nitrogen in the urine represented approximately 45 per cent of that administered. No increase in the excretion of peptides above that excreted on the control regimen was observed following the infusion of Merck's "solution of amino acids mixture, 10 per cent" which is free of peptides. Judged solely from the urinary loss of amino acids and peptides, the authors concluded that a completely hydrolyzed protein appears to be of greater nutritional value than a partially hydrolyzed protein.

Smyth, Levy, and Lasichak studied the wastage of intravenously administered protein hydrolysates and amino acid mixtures due to urinary spillage during the first 4 hours after the infusion was started. Three different preparations were used. One was a 10 per cent solution of an enzymatic hydrolysate of casein (amigen)®, the second was a complete acid hydrolysate of casein fortified with tryptophan (parenamine)®, and the third was a mixture of amino acids prepared by recombination and fortification of fractions of an acid hydrolysate of casein (Merck's VUJN-IX). They were administered to 15 male patients with no detectable metabolic disorders at rates which previous experience had shown to be the maximum tolerated in most patients (5.4 grams nitrogen in 1 to 2 hours). The urinary amino nitrogen values were corrected for corresponding values after an infusion of physiological saline solution. Although there was much individual variation among different patients, by far the greatest urinary wastage of amino acid nitrogen occurred with the enzymatic hydrolysate of casein containing large amounts of peptide nitrogen. The increased loss appeared to be due mainly to "bound" amino acid nitrogen. While from 1.6 to 19.7 per cent of the total administered amino nitrogen was lost in the urine in a 4 hour period following the infusion of

the enzymatic hydrolysate, the loss was usually 3 to 5 per cent with the other two preparations under similar conditions. With all three preparations, there was little free amino acid nitrogen lost, regardless of the speed of infusion. Another interesting observation made was that there was no increase in the urinary wastage of amino acids when the peptide-free Merck preparation was injected at a very rapid rate (500 milliliters of the mixture containing 6 grams of nitrogen was given in 35 minutes instead of the usual 1 to 2 hours). Moreover, such rapid rates of administration produced no ill effects. It should be pointed out that these findings do not necessarily indicate that rapid infusion of amino acids is not wasteful. It is not only the urinary loss of amino acids and peptides, but the loss of urea and ammonia which represents a wastage of injected nitrogen. Indeed, data showing that rapid injection leads to an increased loss of urea is presented below (78).

Silber and Porter (78) studied the percentage of nitrogen retained and amino acids excreted in the urine when 6 different protein hydrolysates were fed to dogs orally and intravenously during 4 day periods. Four preparations contained 37.6, 30, 44.5, and 25 per cent of the total alpha-amino nitrogen as peptides and two preparations were complete hydrolysates. The method of hydrolysis was not mentioned, but was presumably with acid. Adult mongrel dogs, maintained for 2 or 3 weeks on a protein-free diet supplemented with lactalbumin (70 calories and 120 milligrams of nitrogen per kilogram per day) were fed with the hydrolysate orally by stomach tube or by intravenous infusion at a constant rate of 2 milligrams of nitrogen per kilogram per minute, and the lactalbumin was omitted from the diet. The urinary excretion of free amino acids by the dogs was negligible during the periods of oral feedings of all the hydrolysates. After intravenous administration over a period of one hour daily, the urinary loss of free amino acids was in the range from 5 to 20 per cent (average 14 per cent) and there was a corresponding 25 per cent decrease in nitrogen retention with most of the preparations. However, an average of 30 per cent of the peptides was excreted. When the daily allotment was given rapidly by vein in only 15 minutes, the loss of amino acids in the urine increased by a further 10 to 15 per cent, but the nitrogen retention fell approximately 60 per cent obviously because of a greater excretion of urea and ammonia resulting from the deamination of the amino acids. After oral feeding of the peptide-containing preparations, 2 to 11 per cent of the peptide fraction was lost in the urine. Apparently some peptides are absorbed in the gastrointestinal tract before coming in contact with peptidases.

The observation that a four-fold increase in the rate of infusion resulted in no additional loss of peptides in the urine suggests that this loss is not due to a low kidney threshold, but that certain peptides are not retained, irrespective of the rate of infusion, and probably because of their size or composition. This observation, however, is contrary to the findings of Risser *et al.* who found that peptides were lost in increasing amounts at faster rates of infusion.

One preparation containing 44.5 per cent of peptides, which was utilized almost as well as casein when given orally, was found to have no biological value at all in terms of nitrogen retention when administered intravenously (78). While the large quantity of peptides would have been further broken down by the digestive ferments and utilized when given orally, there was excessive urinary loss of the amino acids (12 per cent) and particularly the peptides (45 per cent). Obviously, critical amounts of essential amino acids were lost with the excreted peptides. These results emphasize the necessity of demonstrating that a preparation designed for intravenous use is efficiently utilized when given by this route to the species for which it is intended.

It is pertinent in this connection to refer to the work of Eckhardt and Davidson (23) which suggests that the phenylalanine requirements for nitrogen equilibrium in man are higher when the amino acid solution is given intravenously than when the same solution is given orally. For this investigation these authors used a complete acid hydrolysate of casein from which most of the glutamic and aspartic acids were removed, and which was supplemented with tryptophan, methionine, and glycine. Given in 1 liter quantities to normal human adult males, it supplied from 14 to 15 grams of nitrogen and from 1.7 to 1.9 grams of phenylalanine. On a basal diet supplying 3,000 calories daily and adequate amounts of vitamins and minerals, nitrogen equilibrium was obtained when 1 liter of the solution was given orally in several divided feedings, but negative nitrogen balances resulted when the same solution was given intravenously in one rapid injection, unless it was supplemented orally with about 2.7 grams of L-phenylalanine. An apparently paradoxical situation was observed in regard to the urinary excretion of phenylalanine. When 1 liter of the amino acid solution alone was administered and a negative nitrogen balance resulted, the absolute amount of phenylalanine excreted in the urine and the same expressed as per cent of the amount

present in the infusion were considerably higher than when additional phenylalanine was given orally and nitrogen equilibrium was established. Hier also reported that the excretion of phenylalanine and tyrosine did not decrease, but actually increased when the subjects were transferred from normal diets to low protein diets. These findings are obviously of great practical interest and should be confirmed and extended to include other essential amino acids as well.

The role of the kidney. The question of the urinary loss of essential amino acids following the parenteral administration of protein hydrolysates and amino acid mixtures was approached from a different angle by Wright and his coworkers. They determined the renal clearances of individual essential amino acids in female dogs when the amino acids were administered singly, in pairs, as a mixture of 10 essential amino acids, and as an acid hydrolysate of casein plus tryptophan. The amino acids were given via the radial vein at different rates by means of an electrically driven apparatus permitting constant rates of infusion. Blood samples were obtained from the femoral vein and urine samples were obtained by catheterization. Amino acid concentrations in the plasma and the urine at regular intervals were determined by microbiological methods. Creatinine clearances were determined simultaneously. It was found that amino acids vary with respect to the efficiency of reabsorption following filtration from elevated plasma levels. Eight of the essential amino acids —leucine, isoleucine, valine, methionine, histidine, threonine, phenylalanine, and tryptophan— are reabsorbed well at elevated plasma levels, while arginine and lysine are poorly reabsorbed at elevated plasma levels. Certain amino acids may compete with each other for reabsorption by the renal tubules. Such competition studies have indicated the probable existence of at least 3 functional mechanisms involved in the reabsorption process of amino acids, one reabsorption mechanism being concerned with arginine, histidine, and lysine, a second mechanism with the monoaminomonocarboxylic amino acids, leucine, and isoleucine, and a third group with glycine.

When a mixture of ten essential amino acids, and an acid hydrolysate of casein plus tryptophan were injected at approximately the maximal tolerated rates, the plasma levels of the individual amino acids did not rise high enough for the maximal rates of tubular reabsorption to be exceeded, or for any significant competitive inhibition of reabsorption between different amino acids to occur. This is a finding of practical importance. The maximum rate of infusion used by the authors was 8 milligrams of amino acids per kilogram per minute. This does not, however, seem to be the maximum tolerated rate since other workers (Eckhardt and Davidson, 22) have infused into human subjects Merck's amino acid solution, 10 per cent, at rates as high as 10 milligrams of nitrogen per kilogram per minute (i.e., over 60 milligrams of amino acids per kilogram per minute) without any ill effects.

Evidence of a lower kidney threshold for the unnatural D-forms of amino acids was observed by Silber *et al.* (75) The intravenous infusion of 220 milligrams of nitrogen per kilogram in the form of an amino acid mixture (VUJN) consisting essentially of the L-forms (90 per cent) to normal dogs at a rapid rate of 12 milligrams of nitrogen per kilogram per minute, resulted in the urinary loss of 13 per cent of the alpha-amino nitrogen, while the infusion of a mixture containing 50 per cent racemic amino acids (VUJ mixture) at a similar rate was followed by the loss of 23 per cent in the urine. It was also observed that the urinary excretion of amino acids by dogs given an amino acid mixture intravenously decreased from 30 to 50 per cent during protein depletion. The daily addition of from 10 to 20 grams of casein to the stock diet had no effect on the urinary excretion of alpha-amino nitrogen, but the feeding of 60 grams of casein and 50 grams of meat daily produced a slight increase in the excretion of the infused amino acids. These results suggest that the amino acid excretion after the infusion of a standardized amino acid mixture might be considered the reflection of the state of protein reserves.

A study based upon a concept similar to the vitamin saturation tests was carried out by Silber *et al.* (76) in order to determine the relative needs of the body for the various amino acids. Amino acid mixtures were infused into 2 normal dogs at a rate of 6 milligrams of nitrogen per kilogram per minute and a total nitrogen intake of 200 milligrams of nitrogen per kilogram per day, and the urines were assayed for the essential amino acids by microbiological methods. Approximately 10 per cent of the amino acids administered were excreted in the urine. After the first experiment, the composition of the amino acid mixture was altered on the hypothesis that a disproportionately large excretion of any essential amino acid indicates that it is present in the mixture in excess, and, conversely, a disproportionately low excretion of any amino acid indicates a comparatively small amount of this acid in the mixture. On the basis of this principle, a mixture of amino acids was devised which after infusion into normal dogs at a uniform rate was excreted in practically the same

pattern as that of the infusion mixture. It was assumed that the nearly 90 per cent of the mixture that was retained and had the same pattern as the infused mixture was utilized efficiently by the body. It was observed that some of the amino acids, e.g., threonine, were excreted in larger proportion in the urine regardless of the proportion in the infused mixture. This could possibly be due to a low renal threshold for threonine, although Wright observed that the maximal rates of tubular reabsorption were not even approached when a casein hydrolysate or an amino acid mixture was given intravenously to dogs at about one-fourth the rate of infusion employed in this study. Silber *et al.* (76) hope that this line of approach may be helpful in designing amino acid mixtures "tailored" to suit the needs of specific types of patients.

Studies with pure amino acids. Reference was made earlier to the development by Merck and Company of a "solution of amino acids mixture, 10 per cent" which is free from peptides, practically free from aspartic and glutamic acids, and is richer in essential amino acids (being 64 per cent of the total amino acid mixture). Studies made by Eckhardt and Davidson (21, 22) have demonstrated the practical advantages of this preparation over earlier protein hydrolysates. It was better tolerated in man and in many subjects 500 milliliters (47 grams of amino acids) of the solution could be given in less than an hour (21). Patients with severe active cirrhosis of the liver and infants with infectious diarrhea were among those who tolerated the injections well. In another study (22) 500 milliliters of the solution (47 grams of amino acids) were injected without glucose into 8 normal fasting subjects at three rates of administration, 2, 6, and 10 milligrams of nitrogen per kilogram per minute, representing total infusion times of approximately 60, 20, and 10 minutes, respectively. The initial plasma alpha-amino nitrogen values averaged 3.6 milligrams per 100 milligrams, which rose to 22.5 milligrams per cent 5 minutes after infusion, rapidly fell to 7.2 milligrams per cent 1 hour later, and returned to almost normal by 4 hours. The urinary losses of the infused amino acids were over the range from 1 to 16 per cent for the individual amino acids, an average of 4.3 per cent for the 10 essential amino acids injected and 9.5 per cent of the total alpha-amino nitrogen. The increased excretion of amino acids was completed within 4 hours after the infusion, coinciding with the return to normal of the plasma amino nitrogen values. There was very little increase in the urinary excretion of amino nitrogen after the extremely rapid rates of infusion. Unfortunately, experiments in dogs have shown (78) that at rapid rates of infusion the amino acids are liable to be deaminated and wasted. Further work on this aspect of the problem, however, is clearly indicated. Another interesting observation was that while the essential amino acids constituted 64 per cent of the infused mixture, they formed only 29 per cent of the amino acids excreted. This was interpreted as being due to a preferential retention of the essential amino acids by the subjects, although theoretically it may as well have been due to deamination of a larger part of the essential amino acids. In agreement with other works, it was found that large percentages of the administered threonine and histidine and intermediate percentages of lysine and tryptophan were excreted in the urine.

Harper studied the tolerance of human beings to amino acid given intravenously by rapidly injecting Merck's VUJ-N mixture into normal male subjects at the rate of 1 milliliter per pound of body weight, and determining microbiologically the essential amino acid levels of the plasma at regular intervals and urinary excretion within 3 hours after the infusion. In agreement with other workers (22, 75), it was found that the pattern of amino acids excreted bears no relationship to that infused, and that histidine, lysine, and threonine formed the major part of the excreted essential amino acids. However, the blood levels of most of the amino acids retained a close resemblance to the infusion mixture.

Using quantitative paper chromatographic technique, Awapara and Marvin studied the capacity of the kidney, liver, and muscles to concentrate the amino acids, aspartic acid, glutamic acid, glycine, and alanine when they were singly injected intravenously into male adult rats. The pattern of concentration was found to be characteristic of each organ studied. The kidney was the most active, the liver intermediate, and the muscles were the least active in concentrating the infused amino acids. The results also suggested interconversions of amino acids, possibly by transamination.

Schwerin *et al.* studied the uptake of glutamic acid and glutamine by the brain and other tissues of the rat and the mouse when they were injected intravenously. Both the compounds were found to disappear rapidly from the blood and there was considerable accumulation in the kidney of either one when it was injected. Large amounts of glutamine were taken up by the liver, which was followed by the liberation of glutamic acid. The results suggest that glutamine may enter the brain, but glutamic acid cannot do so. When glutamic acid was injected, its increase in the liver and the

muscles was no more than that resulting from equilibration with the plasma concentration. It seems, therefore, that glutamine is taken up by various tissues more freely than glutamic acid.

As the first of a series of studies planned on the metabolism of parenterally administered amino acids, Handler and his coworkers investigated the effects of injecting glycine into dogs. When administered continuously by the intravenous route in dosages ranging from 0.4 to 1.0 gram of nitrogen per kilogram of body weight, glycine was found lethal to dogs. Symptoms preceding death due to excessive glycine administration were in the following sequence: nausea and vomiting, respiration becoming slow and abdominal in character, respiratory distress, cyanosis, hypothermia, and oliguria or anuria. After the onset of respiratory changes, the discontinuation of infusion and the administration of coramine or adrenalin failed to produce recovery. During the terminal stages, the blood glucose concentration rose and the liver glycogen was low. Glycine alone given over periods of 15 to 18 hours to fasting dogs exerted neither a sparing nor an accelerating effect upon protein catabolism, but there was a sparing action when it was administered together with sufficient glucose to satisfy the caloric needs.

Although it has been shown repeatedly that the intravenous administration of suitable protein hydrolysates or amino acid mixtures leads to positive nitrogen balance, there has been no direct demonstration of tissue protein synthesis from these amino acids. Ross and Elman presented evidence to show the deposition of protein in the liver of dogs following the intravenous injection of a protein hydrolysate (amigen) and glucose. Six adult dogs were put on a protein-free diet for 2 weeks, at the end of which the liver was biopsied for microscopic study and nitrogen determination. Three dogs were maintained over a week on a nitrogen-free regimen while the other 3 received, in addition, amigen infusions to supply 600 milligrams of nitrogen per kilogram per day. At the end of the experiment, it was found that the livers of the dogs receiving protein hydrolysate weighed more than those of the controls receiving only glucose (average of 36.9 and 31.2 grams per kilogram of initial body, respectively). The nitrogen content of the livers showed similar changes (+0.43 per cent and +0.02 per cent, respectively, as compared with the initial levels). Microscopic examination revealed the presence of stainable cytoplasm in the liver of dogs receiving amigen, while the controls showed the vacuolated clear cytoplasm which is characteristic of protein depletion.

The effect of malnutrition. Relatively little is known about the effect of malnutrition on the metabolic processes in the body. By means of isotopic tracer studies, Sanadi and Greenberg showed that the capacity to incorporate labeled amino acids into tissue proteins is impaired in rats maintained on diets deficient in essential amino acids. Young male rats were made deficient in tryptophan and phenylalanine and given test doses of C^{14} labeled tryptophan and glycine, intraperitoneally. After 8 hours, the animals were sacrificed and the concentration of the label in proteins from different organs was determined. The deficient animals had much less of the label in the tissue proteins than the control animals. The results indicate that in essential amino acid deficiency there is a decrease in the net synthesis of protein, or there is a lowered rate of turnover, or both.

Other routes of parenteral administration. Although intravenous infusion is the most common practice, some workers have tried subcutaneous and intramuscular routes and claimed that these procedures have some advantages for the administration of protein hydrolysates and amino acid mixtures. Urwitz gave 240 subcutaneous injections (10, 130 ml.) of an amino acid preparation (aminosol[1]-glucose, containing 3.3 per cent of amino acids and 5 per cent glucose) to 21 children without any complications, the body weights being maintained or increased. Weinstein (86) compared the results of intravenous, subcutaneous, and rapid intramuscular infusions of Baxter's protein hydrolysate, a 5 per cent solution of a pancreatic digest of bovine plasma, in which 50 per cent of the total nitrogen was in the form of free amino acids. In 2,003 consecutive intravenous infusions of 1 liter each at an average rate of 12 to 17 millimeters per minute, in 320 preoperative and postoperative surgical patients, there was only 0.72 per cent of reactions. The hydrolysate was, therefore, considered a safe parenteral fluid. The same hydrolysate was given in 1 liter quantities in 420 subcutaneous infusions at the rate of 6.25 millimeters per minute in 126 patients, and in 170 intramuscular injections at a rate of 3.3 milliliters per minute in 78 patients without failure of absorption, local reactions, or irritation, and with negligible pain or discomfort. From simultaneous clearance studies with phenolsulfonphthalein, the author concludes that nearly all the infused hydrolysate was absorbed 6½ hours after the subcutaneous, and 3 hours after the intramuscular, administrations. However, the conclusion is

[1]Swedish preparation and not the American preparation of the same name.

based on the assumption that the rates of clearance are the same for phenolsulfonphthalein and for amino acids, experimental proof of which is lacking. This author believes that intravenous infusion leads to wastage of the hydrolysate as seen by an increased output of nitrogen in the urine as urea and amino acids, while the slow absorption following subcutaneous or intramuscular infusion supplies the amino acids as they are needed for synthesis. The possible advantages of a slow rate of absorption after subcutaneous or intramuscular administration of amino acid solutions deserve further study. The observation that there was no increase in the urinary excretion of nitrogen or amino acids after the intravenous infusion of 1 liter of the hydrolysate is not in accord with other published work.

In another paper Weinstein (87) described the intramuscular administration of the same Baxter's protein hydrolysate in 254 consecutive injections to 112 postoperative patients. He could simultaneously inject both thighs intramuscularly with 1 liter of a solution containing 80 grams of protein hydrolysate at the rate of 25 to 30 milliliters per minute.

Narat and others found that the intraperitoneal drip method was unsuitable for the administration of protein hydrolysate solutions into rabbits, because the amino acids were not absorbed at all.

Physiological effects and side reactions. Direct evidence showing that the glutamic acid contained in amino acid mixtures is the main agent causing nausea and vomiting on intravenous transfusion was provided by Levy and his coworkers. They determined by microbiological assay a decreasing concentration of free glutamic acid in a number of solutions used in the experiment as follows: a complete acid hydrolysate of casein supplemented with tryptophan, an enzymatic hydrolysate of casein, an enzymatic hydrolysate of beef blood proteins, amino acids from acid hydrolyzed casein, fractionated and recombined, and a mixture of 10 essential amino acids plus glycine. The occurrence of nausea and vomiting after the intravenous administration of these preparations in 57 human subjects was found to parallel the free glutamic acid contents of the mixtures given. In more than half of the subjects, nausea and vomiting occurred when the free glutamic acid content of the serum exceeded 12 to 15 milligrams per 100 milliliters, which showed a direct relationship between the two. When glutamic acid alone, partially neutralized, was injected, fewer patients became ill than when it was given together with other amino acids, which indicated a possible potentiation of the glutamic acid toxicity by the other amino acids. It was further observed that glutamic acid solutions sterilized by Seitz filtration caused more reaction than those sterilized by autoclaving. This difference could not be explained on the basis of the conversion of glutamic acid on autoclaving into pyrrolidone carboxylic acid, because microbiological assay did not indicate such a change.

In view of the wide use of protein hydrolysates in patients undergoing gastric surgery, it is of considerable clinical interest to study the effect of such injections on gastric acidity and motility. Crider and Walker observed the gastric function in a young woman with a large fistula which permitted direct observation of the interior of the stomach. The intravenous administration of a 5 per cent solution of either an enzymatic hydrolysate of casein (amigen) or a solution of crystalline amino acids (Merck's) in 5 per cent dextrose was found to decrease gastric motility and secretion. Such inhibitory effects were not observed during injections of 10 per cent dextrose solution with or without sodium chloride or of isotonic saline solution. It is concluded, therefore, that the intravenous injection of amino acid mixtures depresses gastric function and thus provides gastrointestinal rest.

Zweig and his coworkers obtained slightly different results in a study in which different types of protein hydrolysates (commercial names not mentioned) were given intravenously to patients with normal stomachs as well as patients with peptic ulcer, hypertrophic gastritis, or other conditions. It was observed that while the protein hydrolysate infusions did not affect gastric motility, the gastric acidity was stimulated in 55 per cent of the tests performed. The protein hydrolysates that produced marked stimulation of gastric acidity were found to have relatively higher histamine contents and an acid *p*H near 4.0. It was suggested that these two factors alone, or combined with a direct stimulation on the gastric glands by the hydrolysate itself, were responsible for the observed effect. Vagotomy, thoracic sympathectomy, and splanchnicectomy, or small intravenous doses of atropine sulfate failed to affect this stimulation. There was, however, less gastric stimulation when 5 per cent glucose was given simultaneously than when the amino acid solution was given alone. Rice and his coworkers (62) also observed an increased gastric acidity following intravenous infusions of glucose-amino acid mixtures. It may be that difference in the sex of the patients studied accounts for the findings reported by Crider and Walker, whose patient was a female.

There were two reports on the effect of the parenteral administration of amino acid solutions on food intake. Janowitz and Grossman gave to male adult rats, by intraperitoneal route, a mixture of glucose and protein hydrolysate (amigen) in calorically significant amounts (from 17 to 25 per cent) and found that it did not produce depression of food intake any greater than that produced by saline injections. Mok and his coworkers observed that the intravenous administration of "Amino Acids, I.C., Lyophilized" to 20 patients did not consistently influence the voluntary food intake of calories; in a majority of instances, the food intake either remained stationary or was improved.

The possible antigenicity of partially hydrolyzed protein intended for parenteral use constitutes a real danger. Roth and others investigated the factors influencing the production of anaphylaxis in guinea pigs with weakly antigenic protein hydrolysates and discussed the method for its satisfactory demonstration. It was observed that antigenic substances produced from fibrin by acid hydrolysis may be partially despeciated and may not cross react with the parent material. Ultimately they are destroyed by further, though incomplete, hydrolysis when approximately 55 per cent of the amino acids are liberated.

Duncan and his coworkers studied the effect of total intravenous alimentation on the mineral and bacterial content of the feces. Small amounts of calcium, potassium, phosphorus, and nitrogen were recovered from the colon in enema returns and stool, the largest amounts being recovered from patients experiencing nausea and vomiting. In 5 patients the total number of viable aerobic bacteria recovered from the colon increased during the period of intravenous feeding.

CLINICAL OBSERVATIONS

Value in hepatic disease. Although a liberal intake of protein orally is widely recommended in the treatment of hepatic disorders, particularly cirrhosis of the liver, the question of administering protein hydrolysates intravenously has been a subject of controversy (29), although many clinical reports indicated its safety and therapeutic value. It had been argued that amino acids given parenterally are not promptly utilized or deaminized by the diseased liver and would therefore result in an unusually high incidence of untoward reactions. Moreover, the Council on Pharmacy and Chemistry (60) of the American Medical Association has come to the conclusion that the intravenous injection of amino acids is contraindicated in severe hepatic insufficiency. However, further convincing evidence on the clinical safety and usefulness of amino acids given intravenously in hepatic disease is provided by the careful investigation of Eckhardt and his coworkers (25). Four patients with active cirrhosis of the liver, 3 of them deeply jaundiced, were given intravenously from 50 to 100 grams of amino acids (Merck's "solution of amino acids mixture, 10 per cent") daily for from 2 to 4 weeks as the sole source of nitrogen. The infusions were well tolerated and it was possible to achieve positive nitrogen balances without azotemia or hyperamino acidemia. The urinary loss of amino nitrogen and the pattern of the individual amino acids excreted in the urine were essentially similar to those observed in normal subjects. All of the 4 patients showed clinical improvement as evidenced by a progressive decline in the serum bilirubin, the degree of jaundice, and the bilirubinuria. A decrease in the size of the liver and spleen was seen in 2 patients, and liver biopsy in 1 patient revealed a distinct improvement in the histologic appearance. The results of the study show that amino acids given intravenously are well tolerated by patients with severe liver disease, are metabolized normally, and are clinically beneficial. It was suggested that the adverse results obtained by some of the earlier investigators may have been due to the use of hydrolysates less refined than those available now.

Other observations. Cooper and others investigated the nature of the defect in Wilson's disease (hepatolenticular degeneration) leading to a large urinary excretion of amino acids. The urinary excretion of amino nitrogen in the fasting stage by 6 patients with Wilson's disease was found to be 2 to 3 times that in normal individuals. However, the rapid intravenous injection of 500 milliliters of Merck's 10 per cent solution of amino acids mixture or the oral ingestion of protein foods did not result in further increase in amino acid excretion. There was no excessive excretion of any specific amino acids, nor was there any demonstrable defect in the intermediary metabolism of amino acids. Although the amino acid excretion was strikingly high, it was not considered to be of much nutritional significance since the daily loss was found to be the equivalent of about 3.2 grams of protein.

Sappington and Bockus studied 5 patients suffering from chronic ulcerative colitis and found that all of them had protein deficiency, as indicated by the establishment of positive nitrogen balances on moderately high protein diets. They also expressed the opinion that parenterally administered protein hydrolysate (amigen) was rel-

atively well utilized by these patients and that it was advantageous as a supplement to a high oral intake of protein. The interesting observation was made that the attainment and maintenance of positive nitrogen balance preceded signs of clinical improvement by several weeks in all cases. This work emphasizes the prevalence of protein deficiency in cases of idiopathic ulcerative colitis and suggests that positive nitrogen balance over a long period may be a necessary condition for clinical remission.

Williams and his coworkers gave hydrolyzed casein (casydrol[1] 2½ per cent in 5 per cent glucose) intravenously to 26 infants when oral feeding was stopped because of gastroenteritis, peritonitis, or congenital obstruction of the alimentary tract. The infusions were well tolerated, and in 19 of these infants who survived their disease, evidence of clinical improvement due to parenteral feedings was noted.

Studies after operation. A number of studies have been reported on the postoperative nitrogen loss and the utilization of parenterally administered amino acids by surgical patients. Although there is extensive evidence showing the clinical benefits resulting from the administration of amino acid solutions to surgical patients who cannot eat protein-containing foods for considerable periods of time, some workers (58, 89) believe that the increased nitrogen loss is due to a catabolic reaction to injury and that any additional nitrogen intake in the form of oral protein or parenteral amino acids is only wasted by urinary excretion. Wilkinson *et al.* studied 9 well nourished patients undergoing partial gastrectomy and other surgical operations of similar severity, and observed an absolute increase in the daily urinary nitrogen excretion which lasted from 5 to 8 days with a maximum loss between the second and fifth days. This increased excretion in urine did not occur in persons who did not undergo operation, but in those whose daily protein intake was reduced from 90 to 10 grams. After gastrectomy, 4 patients were given intravenously, every day for 4 or 5 days, protein hydrolysate (casydrol[1]) equivalent to from 80 to 120 grams of protein and from 100 to 150 grams of glucose. These patients excreted more nitrogen in the urine than the controls, the increase being nearly equal to the nitrogen content of the infusion. In another group of 3 patients, 70 grams of protein and 1,800 calories were given daily by way of intrajejunal drip of a mixture of milk, skimmed milk powder, and lactose. The postoperative increase in urinary nitrogen excretion was unaffected, although there was a less severe negative nitrogen balance in this group than in the group receiving protein hydrolysate intravenously. The authors concluded from these experiments that the catabolic phase in the early postoperative period is in no way modified by the oral intake of protein or by the intravenous administration of protein hydrolysate solutions.

Nitrogen balance studies were also carried out by Werner *et al.* on 26 well nourished patients in order to distinguish the effects of the trauma of operation per se and of the usual postoperative reduction in food intake. The patients underwent operations for cholecystectomy, ventral or inguinal hernia repair, and colotomy. In all the patients the protein intake was kept constant within the range from 78 to 90 grams daily. A reduction in the caloric intake in the preoperative period from between 30 and 60 calories to 18 calories per kilogram of body weight produced a sharp negative nitrogen balance. While the patients were on this low caloric and full nitrogen intake (all feedings being parenteral), the surgical operation did not cause any appreciable change in the negative nitrogen balance. Even in patients receiving the required amount of calories and nitrogen all through the preoperative and postoperative periods, no significant changes in nitrogen balance attributable to the surgical procedure were observed. The authors concluded that in these patients "no significant increase in nitrogen output resulted from the operative procedure," and that "simple caloric lack explains the postoperative nitrogen loss found following operation uncomplicated by infection." However, they did not present any data on the daily urinary nitrogen excretion which alone, and not the net nitrogen balance, can reveal possible catabolic effects of the surgical operation, as was emphasized in an earlier paper by Wilkinson *et al.*

Parson and others studied the utilization of intravenously administered amino acids (Merck VUJ-N mixture) by 4 patients following surgery (lobectomy, thyroidectomy and tracheotomy, radical mastectomy). Most of the amino acid nitrogen was retained by all of the patients. The major excretion of amino acids occurred within 4 hours from the beginning of the infusion. There was no significant difference in the amounts or patterns of the amino acids excreted after surgery as compared with the controls. The excretion of urea and ammonia expressed as per cent of the total nitrogen was not significantly altered when the amino acid solution was infused into the patients preoperatively and postoperatively, but the percentage of amino nitrogen excretion tended to

[1]This preparation, an enzymatic hydrolysate of casein, is British, made by Genatosan.

be slightly higher after the operation. The results indicate that the capacity of the body to metabolize a large load of amino acids is not measurably impaired following surgical operations of the type encountered in this investigation. These findings are contradictory to those of Wilkinson *et al.* discussed earlier.

Kremen studied the problem of parenteral nitrogen administration in surgical patients with special reference to the preoperative preparation and as a means of effecting positive nitrogen balances. An acid hydrolysate of casein fortified with tryptophan (parenamine) or an enzymic hydrolysate of casein (amigen) given intravenously in amounts supplying 6 grams of nitrogen daily was found insufficient to bring about a positive nitrogen balance. However, uniformly positive nitrogen balances were obtained by the administration of amigen in amounts of about 18 grams of nitrogen per day. Detailed clinical data were presented on the preparation for operation, over a 7 to 9 day period, of 9 poor risk patients, all of whom had lost 20 to 33 per cent of their normal body weight. These patients received practically all of their nourishment intravenously in the form of amigen and glucose, supplemented with whole blood or plasma transfusions. All the patients survived operations of major magnitude with no more complications than are met with in well nourished surgical patients. The author concluded that, from a nutritional viewpoint, the transfusion of whole blood and the administration of casein hydrolysate or amino acid solutions together is a more efficient procedure than the use of either procedure alone.

The great differences in the findings of nitrogen balance after operation as influenced by the intravenous administration of amino acid mixtures are not surprising when we realize the variations in the number of factors influencing the patient. A few of these are the type of operation, the kind of anesthesia, the amount and kind of postoperative medication, the sex of the patient, the previous nutritional status of the patient, his present nutritional status, particularly the relative amount of adipose tissue, and the intensity of the pituitary-adrenal reaction. Further studies of these various factors will undoubtedly give answers to some of these questions.

The careful studies of Cole *et al.* and Keeton *et al.* on postoperative convalescence are of great clinical interest and are pertinent to this review, although they used protein hydrolysate (2 liters of 5 per cent amigen plus 5 per cent glucose) intravenously only on the day of the operation, intact protein being given by tube on other days. Nitrogen balance studies and a variety of physiological tests were performed on 92 patients undergoing herniotomies, and 10 patients undergoing cholecystectomies, and some interesting general conclusions were drawn. The best results were obtained when a high protein diet was given together with adequate calories. A high caloric intake itself did not improve the test performances; in fact, it appeared distinctly to be detrimental. The physiological tests showed a better performance when the full diet (from basal calories plus 20 per cent to basal calories plus 100 per cent and about 2.7 grams of protein per kilogram body weight) was started promptly on the day of operation and continued during the postoperative period, than when the conventional diet of one-fourth, one-half, three-fourths, and four-fourths of the full diet was given during the first postoperative days, respectively. Keeton *et al.* observed that even patients receiving generous supplies of protein went into negative nitrogen balance on the first and second postoperative days although they were in positive balance on the day of the operation. After this period of wastage had passed, the patients were found to behave normally with respect to the conservation of nitrogen. The authors emphasize the fact that this period may be of such short duration as to be obscured by its inclusion in a longer collection period. This may explain why Weinstein (86) *et al.* did not observe any nitrogen wastage in postoperative patients receiving adequate calories and protein. Although there is an inevitable period of nitrogen wastage in the early postoperative period, Keeton *et al.* were able to achieve a net positive nitrogen balance over the period covered by the day of surgery and the 5 following days by the administration (by tube) of a diet furnishing maintenance calories (basal plus 20 per cent) or excessive calories (basal plus 100 per cent) and about 2.6 grams of protein per kilogram of body weight.

The author expresses grateful appreciation of the constant encouragement and valuable suggestions given by Dr. Robert Elman in the preparation of this review. Thanks are due to T. E. Weichselbaum, Ph.D., for his help in securing some of the data presented in the review.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Familial Incidence of Bilateral Giant-Cell Tumors of the Jaw. CHARLES A. WALDRON. *Oral Surg.*, 1951, 4: 198.

The author presents the case of a 7 year old girl with a bilateral swelling of the mandible in the region of the angle of the jaw, of 2 years' duration. Radiologically, each of these lesions was seen as a large multiocular cyst. Treatment by curettage and cautery was administered, and on section each lesion was found to be a benign tumor. Seventeen years later the patient was well and apparently free from disease.

Some years later her sister, younger by 4 years, was brought in for treatment at the age of 9 years, with identical swellings of the jaw, again bilateral, and again of 2 years' duration. The clinical, radiological, and histological findings were precisely the same as those found in the elder sister. Treatment was again by excision and curettage, but just over 5 years later there was a recurrence on one side and similar treatment by limited surgery was administered.

The first patient married at the age of about 21 years and had a female child. Soon after the second birthday, this child too developed a swelling over the angle of the jaw on each side. X-ray films again showed large regular cystic areas in bone. Treatment, as before, was by curettage and cautery. On section these lesions proved to be benign giant-cell tumors. Bilateral recurrence, 2 years later, was treated by limited surgery.

Complete biochemical investigation of the second and third cases failed to show any evidence of parathyroid dysfunction, or any other general disturbance of bone metabolism. M. R. EWING, M.D.

Papillary Cystadenoma Lymphomatosum of the Parotid Gland. ROBERT E. HOLMBERG and DONALD M. GLOVER. *Surgery*, 1951, 29: 240.

Papillary cystadenoma lymphomatosum is an uncommon tumor of the salivary glands, occurring most commonly in the tail of the parotid gland, below the angle of the mandible, and rarely in the submaxillary gland. Known also by other names, it is usually, and perhaps always, benign. Most commonly it occurs in middle aged or elderly males; the condition is relatively uncommon in females and seldom occurs in childhood. Grossly, the tumors are tightly encapsulated, oval, lobulated, and moderately firm. They are easily incised and the cut surfaces are finely granular, but there may be small cystic areas filled with serous or mucinous material. Microscopically, these appear as a series of tubular glands on delicate, branching, papillary stalks which are arranged in lymphoid stroma usually containing germinal centers. The glands are lined by a double row of columnar cells which contain pale-staining cytoplasm and hyperchromic nuclei. The nuclei of the inner row of cells are displaced toward the lumen. The outer cells are frequently cuboidal. Cyst-like spaces are often found.

The usual symptomatology is that of a painless swelling. The tumors are slow-growing and do not recur after complete removal. Upon external examination there is nothing that distinguishes them from mixed tumors. Many theories have been advanced as to the origin of these tumors. They may arise from heterotopias of pharyngeal entodermal anlage into lymph nodes in the vicinity of the parotid gland, aberrant anlages of the eustachian tube, remnants of the branchial arch, orbital inclusion cysts, onkocytes (peculiar cells of the parotid ducts or alveoli), misplaced thymic anlage, lymph vessel endothelium undergoing metaplasia, embryonal rests of ectoderm, and salivary ducts.

The authors recommend the surgical removal of all salivary tumors since identification by clinical criteria is impossible. The majority of the salivary tumors can be removed without injury to the facial nerve.

Irradiation has no significant effect on papillary cystadenoma and should not be used since it complicates surgical therapy. It is important that papillary cystadenoma lymphomatosum be recognized, since that diagnosis confers a much better prognosis than do any of the other common salivary tumors. Because it is usually impossible to distinguish grossly between a mixed tumor and a papillary cystadenoma, all parotid tumors should be removed without injuring the capsules.

The authors add 8 cases of papillary cystadenoma of the salivary glands to the 151 cases collected from the literature. JACOB T. BRADSHER, JR., M.D.

EYE

A Simple Method for the Repair of Full-Thickness Defects of the Lower Lid with Special Reference to the Treatment of Neoplasms. W. M. MANCHESTER. *Brit. J. Plast. Surg.*, 1951, 3: 252.

The author advocates a simple method for the repair of full-thickness defects of the lower eyelid with special reference to the treatment of neoplasms.

Removal of neoplasms of the lower eyelid for basal cell carcinoma and squamous cell carcinoma result in a marginal defect which is difficult to repair.

Many procedures have been described for the reconstruction of a full thickness defect of the eyelid. The ideal method should replace skin, eyelashes, muscle, tarsus, and conjunctiva. This ideal is difficult to achieve. The method suggested by Manchester provides a lining of conjunctiva and a cover of eyelid skin, but without tarsal plate or eyelashes.

After a portion of the eyelid is excised through its whole thickness, allowing a margin of ¼ inch on all sides of the lesion, a conjunctival flap corresponding in width to the defect is freed from the lower fornix and lower bulbar conjunctiva. The flap is folded on itself to recreate the fornix at a slightly higher level than that which remains untouched on either side. The flap is secured at each corner by a single black silk stitch. The skin is then repaired by means of a double-pedicled flap of the Tripier type, prepared from the upper eyelid.

Two series of stitches are used—one to unite the upper border of the skin to the conjunctival flap, and the other to unite its lower border to the remaining eyelid skin. These are tied to each other over a tiny stent mould and the defect in the upper eyelid is closed by sutures.

JOSHUA ZUCKERMAN, M. D.

Oblique Muscle Surgery from the Anatomic Viewpoint. WALTER H. FINK. *Am. J. Ophth.*, 1951, 34: 261.

Surgery on the superior oblique should be confined to the reflected tendon and its insertion. The most efficient procedure for weakening the muscle is tenotomy of the reflected tendon at the nasal border of the superior rectus. In the "eyes front" position the tendon of the superior oblique passes 2 to 3 mm. posterior to the nasal insertion of the superior rectus. A sharp-pointed small strabismus hook (O'Connor) is held flat and snug against the sclera as it is passed backward 1 cm. The point is turned upward and then brought forward to engage the tendon and its sheath. A complete tenotomy between the hook and the superior rectus will take care of 5 to 10 prism diopters of deviation in the primary position. For a deviation of 10 to 20 prism diopters, 3 to 5 mm. of tendon is removed, and for 20 to 30 prism diopters, a removal of 5 to 8 mm. is indicated.

Underactivity of the superior oblique is correctable by a tuck for a moderate effect, and by resection for a greater change. The isolated reflected tendon and its surrounding sheath are placed in the tucker. The tuck should total 5 to 10 mm. Thorough scraping of the contact surfaces will insure firmer healing. A tuck of 5 mm. will probably correct 5 prism diopters of deviation in the primary position; and a 10 mm. tuck, a deviation of 10 to 12 prism diopters. Resection, which is described, is more difficult and causes a greater tissue reaction but gives a greater and more consistent result.

In surgery of the inferior oblique the insertion of the muscle, rather than its origin, is the logical approach. The anterior tip of the inferior oblique insertion is about 9.5 mm. posterior to the lower insertion of the lateral rectus and 2 mm. above. In recession of the muscle the conjunctival incision begins 6 mm. lateral to the upper insertion of the lateral rectus and extends downward about 15 mm. The fascia along the lower edge of the lateral rectus is incised and the muscle is retracted upward. The strabismus hook passes a few millimeters below the border of the lateral rectus with its point directed upward. A muscle forceps is applied close to the scleral insertion and the muscle is severed; the muscle is then retracted outward and its posterior fascial margin is cut. For an 8 mm. recession the new anterior insertion should be 6 mm. below the lateral rectus insertion. This point is marked by gentian violet. The posterior insertion should be 6 mm. posterior to this point. The recession should be 5, 8, or 10 mm., according to the effect desired.

Underactivity of the inferior oblique is efficiently treated by advancement, or resection and advancement of the insertion. Advancing the insertion 5 mm. above the original position will produce a moderate change. If a greater effect is needed the advancement should be combined with a 5 mm. resection of the muscle.

The surgical anatomy as well as the operative details are minutely described and adequately illustrated. JAMES E. LEBENSOHN, M.D.

Reaction of Corneal Nerve Fibers to Injury. E. ZANDER and G. WEDDELL. *Brit. J. Ophth.*, 1951, 35: 61.

These authors have studied the reaction of corneal nerve fibers to injury. It was found that the rate of nerve degeneration and regeneration in the rabbit's cornea are similar to that in the skin of the rabbit's ear.

Regenerating nerve fibers in the cornea pursue their way as easily when unrelated to Schwann cells as when related to them.

A single corneal nerve fiber is distributed over at least a quadrant of the cornea. After denervation, Schwann cells and corneal corpuscles undergo characteristic changes. After keratotomy, the denervated area is re-innervated from three sources: (1) regenerating nerve fibers which penetrate the scar, (2) those which pass around the lateral margins of the scar, and (3) invading fibers which sprout from surrounding normal nerve fibers to invade the denervated area.

There is evidence of active degeneration as well as regeneration of the nerves from the fiftieth to the one-hundred and twentieth day following keratotomy.

Histologic examination reveals that recovery is nearly complete, 220 days after keratotomy. The rabbit's cornea is probably supplied solely by axons from the fifth cranial nerve reaching the cornea by way of the ciliary nerves.

Five days after extirpation of the gasserian ganglion, only degenerating nerve fibers are visible throughout the cornea; 3 weeks after extirpation, regenerating nerve fibers become visible in the insensitive cornea. JOSHUA ZUCKERMAN, M. D.

Nerve Regeneration in Corneal Grafts in the Rabbit. URSULA REXED. *Brit. J. Ophth.*, 1951, 35: 89.

The regeneration of nerves in corneal grafts in the rabbit is discussed. The author found that, except for certain differences, the course and pattern of nerve regeneration in corneal grafts is similar to that which occurs after simple severance of the corneal nerves.

Degeneration and regeneration of the nerves was studied in 23 corneal grafts in the rabbit. The return of sensitivity was followed and silver-impregnated sections were made after periods of from 1 day to 7½ months following operation.

In young animals the peripheral parts of the graft became partly sensitive after 3 to 4 weeks; in adult animals, after 5 to 7 weeks. In young animals the graft became fully sensitive after 4 to 7 weeks; in adult animals, after 10 to 13 weeks.

The processes of degeneration were completed after 7 days.

Regenerated nerve fibers started to cross the scar and grow into the graft after 3 to 5 weeks; after 3 to 7 months mature fibers were found throughout the whole graft.

No proliferation of the Schwann cells could be demonstrated in the cornea of the host or in the graft. It was proved that parts of the original graft still remain after 6 to 7 months.

The new neurites grow out from the cut end of the nerve in the cornea of the host and grow naked through the scar, then they either grow into and re-innervate an empty Schwann sheath or grow on naked towards the center of the graft. The nerve fibers are more numerous than in a corresponding area of normal cornea.

Subepithelial nerve fibers can be seen in clear or cloudy grafts as early as 5 weeks. The ingrowth of nerves did not depend upon the ingrowth of blood vessels.

The process of degeneration and regeneration of the corneal nerves was identical in clear and in cloudy grafts. JOSHUA ZUCKERMAN, M. D.

Surgery of the Lens in Infancy and Childhood. PAUL A. CHANDLER. *Arch. Ophth.*, Chic., 1951, 45: 125.

The author discusses the surgical procedures advocated for disorders of the lens in infancy and childhood, such as congenital cataract, traumatic cataract, cataract associated with uveitis, congenital dislocation of the lens, and microphakia.

Congenital cataracts include bilateral complete cataract, either present at birth or developing during the first few months of life; severe involvement of both eyes without complete opacification of the lenses, as in large and very dense zonular cataracts; mild involvement of the lens of one eye and severe involvement of the other; bilateral dense central opacities, allowing adequate vision with dilated pupils but inadequate vision when the pupils are small; and moderate involvement of both eyes.

The usual operations employed are simple discission, through and through discission, discission followed by linear extraction alone, linear extraction alone, linear extraction with iridectomy and optical iridectomy. The chief complications are glaucoma, an inadequate pupillary opening, and detachment of the retina. Less frequent complications are uveitis, epithelization of the anterior chamber, and corneal edema with bullous keratitis.

For congenital cataract no one operation is recommended to the exclusion of all others, but the importance of the long-continued postoperative use of atropine or scopolamine to avoid posterior synechias is emphasized.

Traumatic cataract is generally the result of a perforating wound of the anterior segment. Unless severe glaucoma develops, surgical treatment should be postponed because complete absorption of the lens may result spontaneously.

Cataract associated with uveitis in children may result in opacification of the lens or the development of a pupillary membrane which reduces vision. Intracapsular extraction with an iridectomy and inferior iridotomy is advocated.

JOSHUA ZUCKERMAN, M.D.

Effect of Cortisone on Horse Serum Uveitis in Rabbits. ALBERT C. BIEGEL. *Arch. Ophth.*, Chic., 1951, 45: 258.

The present study was directed to an evaluation of the clinical and histopathological effects of systemic administration of cortisone on the uveitis produced by the intravitreal injection of horse serum in previously sensitized rabbits. Clinical and pathological study indicated no statistical difference between the treated and control animals within 48 hours of the intraocular injection. In animals studied 9 days after injection, the cortisone treated group showed a striking inhibition of vitreous haze, and suppression of the cellular deposits and fibrin on the anterior lens capsule. Histopathologic study confirmed the clinical observations.

FRANK W. NEWELL, M. D.

Chorionepithelioma of the Choroid; Metastatic from Tumor in Testicle. MAX M. KULVIN. *Am. J. Ophth.*, 1951, 34: 217.

Chorionepithelioma occurs in but 1.5 per cent of testicular tumors. Metastasis to the choroid is exceedingly rare, the report of Kulvin being the fifth recorded case.

A 22 year old white male entered the U. S. Veterans Hospital, Hines, Illinois, complaining of a productive cough and pain in the left flank for 6 weeks, and a loss of 7 pounds in the previous 3 weeks. His left testicle had been removed for adenocarcinoma the year before, after which x-ray treatment to the left groin was given for 2 months. Physical examination revealed a large, slightly tender mass towards the medial side of the left upper quadrant of the abdomen. A mass could also be palpated through the rectum. The urine showed a low concentration of estrogens. Intravenous pyelography demonstrated a nonfunctioning left kidney. After 2 months of deep

x-ray therapy he left, only to return 2 months later when a small, smooth, nontender mass was felt in the suprasternal notch. In exploratory laparotomy a firm mass, 5 x 8 cm., was seen adherent to the vertebral column, aorta, and hilum of the kidney. Biopsy revealed metastatic embryonal carcinoma.

Ten days after operation the patient reported dimness of vision and severe occipital headache. The acuity was R. 20/15; L. 20/1600; ocular tension normal in both eyes. The field of the right eye was full, that of the left eye had a defect nasally and inferotemporally. The right fundus was normal, but the left fundus showed a metastatic tumor in the choroid with detachment of the retina. Transillumination, however, was good.

Death occurred a month later. The findings at autopsy were: an enlarged liver with numerous metastatic nodules; multiple nodules throughout the lungs; lymph nodes infiltrated by tumor cells; and an extensive tumor in the testicle. Histologic study of the eye confirmed the diagnosis of metastatic chorionepithelioma. The article is profusely illustrated. JAMES E. LEBENSOHN, M.D.

EAR

Cholesteatomatous Cysts Secondary to Incomplete Removal of the Cholesteatomatous Matrix. JOSEPH W. BEGLEY, JR., and HENRY L. WILLIAMS. *Arch. Otolar.*, Chic., 1951, 53: 147.

Although external cholesteatomatous cysts of the mastoid developing subsequent to radical operations for the removal of aural cholesteatomas are unusual, the authors believe that the occurrence of this complication constitutes a reason for the complete removal of the cholesteatomatous matrix in the surgical treatment of cholesteatomas of the middle ear and mastoid.

Reports are included in 2 instances of external cholesteatomatous cysts of the mastoid encountered at the Mayo Clinic. In each instance the lesions developed after radical operations for the removal of aural cholesteatomas.

The cysts apparently resulted from remaining cholesteatomatous matrix which formed an evagination, continued to desquamate, enlarged, and expanded in the path of least resistance, which was through the soft tissues into the postauricular subcutaneous tissue.

In opposition to the theory of Tumarkin, the lining of a cholesteatoma has been demonstrated to be true stratified squamous epithelium. Nevertheless, when it is preserved as an epithelial lining, its behavior is different from that of a skin graft utilized to line a tympanomastoid cavity. Whereas the cholesteatomatous matrix may force itself into the haversian canals of bone, form folds and convolutions, and persist in an eczematoid reaction to irritation, a skin graft presents fewer of these potential complications. In certain instances, on the other hand, it has seemed that the eventual result is better when skin grafting is not used, because of occasional tendencies in the grafted skin for an eczematoid reaction to develop. The authors were of the opinion that had the cholesteatomatous matrix been completely removed at the first operation in the cases they presented, there would have been no formation of cysts and no necessity for secondary surgical procedures.

To be considered in the differential diagnosis of these lesions are meningoceles, sebaceous cysts, cystic hygromas, lymphomas, and fibromas. Needle aspiration of the postauricular enlargement, and examination of the aspirated contents may be deemed advisable as a preliminary step in establishment of a diagnosis.

NOSE AND SINUSES

Physiological Principles in Rhinoplasty. SAMUEL FOMON, WILLIAM Y. SAYAD, ALFRED SCHATTNER, and HARRY NEIVERT. *Arch. Otolar.*, Chic., 1951, 53: 256.

Knowledge of nasal physiology is just as important as of the anatomy of the nose and pathological states that can be found there. The nose can not be considered an isolated organ, but a link in the chain of tissue ventilation.

Phylogenetically, the original function of the nose was solely olfaction. In man, upon assuming the upright position, the olfactory organ lost considerable importance. Had the nares remained in a forward position, thus causing a vertical stream of air to pass through the nose, the respiratory air current would have been too low to reach the olfactory area, but during evolution, growth of the nasal cartilages changed the position of the nares to the dependent position.

From a functional standpoint, no interference with nasal breathing will occur if a normal relationship exists between the shape of the nares and the external nasal pyramid. If there is an abnormal relationship between these, a misdirection of air current will occur. If the nasal tip is unduly depressed, the current will be directed toward the dorsum of the nose and shunted backward to form a whirl. This causes drying and crusting of the nasal mucosa. If the tip of the nose is overly elevated the current is flattened and takes a more direct course through the nasal chamber. This also causes drying. In rhinoplasty procedures, if the shape of the nares is changed, the external nasal pyramid must be correspondingly corrected.

Constriction of the nares will interfere with nasal function. An increased negative pressure above the stenotic area results on inspiration, because air fails to enter rapidly enough to equalize pressures.

The size and shape of the bony nasal pyramid has important bearing on nasal physiology. During evolution, the superior maxilla became less important. As a result, the development of the bony nasal pyramid assumes its ultimate shape relatively late. The shape of the external nose is an index to the contour of the underlying cavity; thus, any deviation of the external nose from the normal must

necessarily disturb the cause of the respiratory current and alter the nasal pressures. The respiratory current normally describes a parabolic curve, with an arch of the current upward from the inlet.

Any factor which narrows the nasal canal will accentuate the positive and negative pressure and, conversely, any widening of the canal will diminish pressures. An increased pressure will cause anemia of the mucosa while a decreased pressure will lead to edema and extravasation. These same alterations in pressure may also affect the ventilation of the paranasal sinuses and the middle ear by influencing the sinus ostia or the eustachian tube orifice.

The nose prevents hyperventilation or hypoventilation and offers aid to the cardiovascular system. These physiological principles are best understood when the ventilatory, respiratory, and circulatory phases of nasal respiration, as presented by Best and Taylor, are reviewed.

Restoration of function is an important feature of rhinoplasty, especially if there is any tendency to nasal obstruction. The type of obstruction must be determined. It may be inspiratory due to a collapsing ala, expiratory as found in ball-valve polyps, or combined, as seen in patients with a deviated septum. Systemic conditions such as allergic reactions, cardiovascular difficulties, or dietary deficiencies may cause nasal obstruction and must be ruled out. The cause of the obstruction may be in the upper lateral cartilages, lower lateral cartilages, the connecting aponeurosis, the septum, or in the shape and inclination of the nares.

A great aid to the rhinologist would be a test to check nasal function. Some means similar to those used by thoracic surgeons to test pulmonary function would help measurably. Unfortunately, as yet, no such assistance has been found.

JOHN R. LINDSAY, M. D.

MOUTH

Complicated Fractures of the Maxilla. DAVID L. MURPHY, EDWARD S. MURPHY, and WILLIAM A. MCNICHOLS. *J. Am. M. Ass.*, 1951, 145: 614.

Deforming fractures of the maxilla are often overlooked at the time of the injury, because of swelling. Delayed surgery, however, is only partially satisfactory.

The diagnosis is made by inspection, palpation, and roentgenography. Inspection may not yield a diagnosis if there is too much swelling. Continued observation may suggest a fracture, if a sagging eye-diplopia, or an off-side bite appears. Elevations, depressions, and separations can often be felt. Roentgenograms will often show the fracture but it is possible to be misled if the films are taken at the wrong angle, or if only portions of the bones are present on the films.

Complicated fractures of the maxilla are those which are compound or which involve the alveolar processes, or the orbit, or any combination of these injuries.

Transverse fractures of the maxilla are the easiest to handle. If the alveolar process or palate is fractured too, the oral surgeon is indispensable. Use of the Straith mouthpiece, some dental compound, and a Straith headboard boxed in plaster can often be used to advantage.

A simple depressed fracture of the zygomatic arch may be approached by the temporal or oral route.

Maxillomalar fractures are the most difficult to treat; it is necessary not only to reduce them but also to support them. In these fractures, the suspensory ligament of Lockwood is often torn with resulting diplopia. In order to get satisfactory results in complicated maxillary fractures, a radical maxillary sinusotomy (Caldwell Luc) is done. The orbital wall, the anterior wall, and the hard palate can all be reduced with this procedure. If support is then needed, Stader pins can be inserted into the bone fragments and immobilized to the Straith headboard, or by crosspiece extensions to Stader pins in the unaffected side.

Fractures of the mandible can be effectively treated with external appliances and pin-fixation. Only when the condyle is broken so short that pins cannot be inserted is this method unpractical. In such a case, open reduction with interosseous wiring is indicated. The possibility of ankylosis of the temporomandibular joint is not uncommon following such a procedure.

An interesting case of maxillary fracture was that in a man, aged 42, who was seriously injured in an automobile accident. He was unconscious for 6 days with a depressed fracture of the left frontal part of the skull. There was also a fracture dislocation of the orbital portion of the left malar prominence, the left infraorbital ridge, the left part of the orbital floor, and the left anterior wall of the maxillary sinus. On the eighth day the skull fracture was reduced. After this, the patient continued to have a sagging eye, marked diplopia, and a flat face. On the eighteenth day a pin was placed in the left infraorbital ridge and another one was placed in the left zygoma; then two pins were placed in the right infraorbital ridge. These were used as an anchor for extension rods, to keep the depressed fracture in extension. By means of a Caldwell-Luc approach, the orbital floor was reduced, as was the anterior wall, and held by dry packing. The zygoma was then pulled forward and held by extension rods for 21 days. Packing was removed in 8 days.

JOHN R. LINDSAY, M.D.

Submandibular Flap. J. G. KOSTRUBALA and R. F. STOKES. *Arch. Otolar.*, Chic., 1951, 53: 285.

Repair of facial defects are dependent on many factors. The repaired area should have the color and texture that resembles the normal tissue of that organ; also, visible scars of the donor site must be kept at a minimum to avoid a cosmetic defect as severe as the original produced.

Extensive defects of the upper or lower lip and defects of the cheek can be repaired satisfactorily

by means of a bipedicle submandibular flap. The color and texture requirements are met and the residual scar of the donor site corresponds with a normal skin crease. Redundant chins are often improved in this procedure.

The blood supply to the skin of the submandibular area is supplied through terminal branches of the submental artery, sternocleidomastoid artery, and branches of the thyrocervical plexus. No vessels course transversely in this area and viability of the flap is dependent on the rich anastomosis in the dermal and subdermal plexus.

The technique is as follows: two incisions are made transversely in the submandibular region. The distance between the incisions is determined by the width of the defect to be repaired. The superior incision begins 1 cm. behind and below the angle of the mandible, and is carried forward and around the neck to a corresponding point on the opposite side. The second incision runs parallel to the original incision at a predetermined distance below it. The flap is undermined superficial to the platysma muscle. The central portion of the flap may be lined with a split thickness graft to provide the lining for the newly constructed lip. The entire flap is then resutured to its bed.

The next step is raising the flap and laying it in its new position. The split thickness graft is sutured to the oral mucosa bordering the defect, and the skin is sutured to the face. The raw ends of the central portion are sutured to the freshened lateral skin margins of the defect. The pedicles are then amputated at their origins and the wound closed.

In repairing a lip, the vermilion border is lacking but is usually not wished for by patients. Tattooing has helped in cases in which it is desired.

JOHN R. LINDSAY, M. D.

NECK

Treatment of Hyperthyroidism (Traitement de l'hyperthyroidie). R. DUPÉRIÉ. *J. méd. Bordeaux*, 1950, 128: 96.

The storage of inorganic iodine by the thyroid tissue is inhibited by thiocyanates. A concentration of iodine in the plasma above normal levels inhibits the thyroid function.

Tyrosine, an amino acid furnished by food, combines within the thyroid tissue with iodine to form iodotyrosine. The iodine necessary for this process is liberated from alkaline iodides by an enzymatic oxidation produced by chrome-oxidase and peroxidase. Cyanides, sulfides, and thiouracil inhibit cytochrome oxidase and thus interfere with the formation of iodotyrosine. Thiourea inhibits in vitro the specific action of peroxidase. Sulfathiazole, para-aminobenzoic acid, and aniline derivatives depress the production of thyroxin by competing for iodine.

Metallic iodine combines with tyrosine to form, first, monoiodotyrosine and then diiodotyrosine. Two molecules of the latter unite by oxidation to form one molecule of thyroxin. Radioactive iodine, aminothiazole, thiourea, thiouracil, amidazol, and sulfonamides inhibit this process.

Thyroxin participates in the formation of thyroglobulin, the main component of the colloid. Products of hydrolysis of thyroglobulin constitute the thyroid hormone circulating in the blood. The only known inhibitor of this stage is an excessive amount of iodine in the plasma.

The circulating thyroid hormone, thyroxin, exerts a specific metabolic effect on various organs. Certain conditions of the bone marrow, such as anemia, leucopenia, or agranulocytosis, those of the liver, such as jaundice, or conditions of the nervous system, such as hyperthermia, counteract the effect of thyroxin.

This brief review shows that certain antithyroid agents affect several stages of thyroxin secretion. For instance, iodine inhibits the storage by the thyroid gland of this metal circulating in the blood; it interferes with the formation of thyroxin and with the action of proteolytic enzymes responsible for liberation and circulation of the thyroid hormone; and finally, an excess of iodine inactivates the pituitary thyrotropic hormone.

The thyroid activity is dominated by thyrostimuline, which is secreted by the anterior lobe of the hypophysis. A disturbance of the pituitary thyroid equilibrium by antithyroid agents produces changes macroscopically, such as hypertrophy of the thyroid gland, and microscopic visible lesions such as vacuolization and loss of staining qualities of the colloid.

The gonads, especially the ovaries, participate in this glandular interaction. It follows that the medical treatment of hyperthyroidism may be directed toward the thyroid gland, the hypophysis, or the gonads.

JOSEPH K. NARAT, M.D.

The Problem of Thyroid Carcinoma. WILLIAM H. PERLOFF and NORMAN G. SCHNEEBERG. *Surgery*, 1951, 29: 572.

The records of all patients hospitalized in the Philadelphia General Hospital from 1936 to 1946 were analyzed. Microscopic slides from the surgical or autopsy specimens were sent to 6 pathologists in different institutions for their diagnostic opinions.

Forty-nine cases of thyroid malignancy are recorded in this group; 15 of these cases were discarded because the diagnosis could not be established either microscopically or clinically. Using this as a basis, 5.2 per cent of all nontoxic nodular and adenomatous goiters were considered to be malignant. Among the 30 cases of supposedly primary thyroid carcinoma, the consulting pathologists concurred in this diagnosis in only 12 of 22 instances. In 1 case they all agreed upon the benign nature of the lesion. In another case, 4 pathologists considered the lesion benign and 2 thought it malignant; 1 was doubtful. In a third case, only 1 of the 7 pathologists considered the lesion benign. The average of these 7 opinions is 3.2 per cent, representing a reduction of 38 per cent in the computed incidence of primary thyroid carcinoma.

Three reported cases in which there was primary and metastatic carcinoma of the thyroid are presented. In the discussion, it is brought out that the percentage incidence of thyroid malignancy encountered at Philadelphia General Hospital, Johns Hopkins Hospital, and Massachusetts General Hospital is 3, 9, and 10 times, respectively, greater than that reported at Boston City Hospital. The incidence of multinodular malignant goiters varies from 4.5 per cent to 11 per cent. Opinions also vary; there are those who advocate wholesale removal of all nontoxic goiters and those who believe that such prophylactic surgery is completely unnecessary. Agreement among the pathologists varied from 69 per cent to 82 per cent, and pathologic criteria of thyroid malignancy in nontoxic nodular and adenomatous goiters are not yet firmly established.

RICHARD J. BENNETT, JR., M. D.

Sarcoma of the Larynx. JOSEPH LACHMANN. *Arch. Otolar.*, Chic., 1951, 53: 299.

Two cases of sarcoma of the larynx are reported.

The first patient was a male aged 52 years, who, when first seen, had been suffering from hoarseness for a period of 1 year. Examination revealed a big subglottic tumor arising from the anterior wall of the larynx. An acute emergency tracheotomy was performed, followed in 4 weeks by a thyrotomy. The histologic diagnosis was polymorphocellular sarcoma arising from fibrosarcoma. The patient received radium treatment of 7,650 roentgens in 40 sittings. Six years after operation there was no record of the tumor.

The second patient was a male, aged 63 years, who revealed a tumor of the left vocal cord extending from the anterior commissure to the arytenoid region. After an inferior tracheotomy, a subtotal hemilaryngectomy (left) was performed. The histological diagnosis was lymphosarcoma. The patient died on the ninth day after operation from an embolism of the pulmonary artery due to thrombosis of the left femoral vein.

The author notes that in the radium department of his hospital, 190 malignant tumors of the larynx were treated in 13 years, 2 of which were sarcomas.

RICHARD J. BENNETT, JR., M. D.

Operation for Zenker's Terminal Diverticulum (Zur Operation der Zenkerschen Grenzdivertikel). FRITZ HAAS. *Wien. med. Wschr.*, 1951, 101: 74.

The aim of a successful operation for Zenker's diverticulum is not only elimination of the pathologic formation, but also restitution of the normal function, which in turn depends on proper anatomic conditions.

Palliative operations, such as transposition or invagination of the sac, even if supplemented by excision in the second stage, fail to reconstruct the wall of the esophagus. Only excision of the diverticulum in one or two stages, with an immediate plastic reconstruction of the esophageal wall, meets the requirement of restitution of normal conditions.

The author describes a method which permits the reconstruction of the cricopharyngeal muscle and which furnished very satisfactory results in 8 cases. The most important step of the operation consists in suturing the esophageal mucosa in transverse direction after excision of the diverticulum, and of plication of the separated fibers of the cricopharyngeal muscle in 2 rows. This method restores the normal position of the muscle and prevents recurrences.

JOSEPH K. NARAT, M.D.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Hydrocephalus Due to Intrinsic Stenosis of the Aqueduct of Sylvius, Based on 19 Cases Observed at the Neurosurgical Clinic of Pitie from 1928 to 1950 (Les hydrocéphalies par sténosa intrinsèque de l'aqueduc de Sylvius, D'après 19 cas observés à la clinique neurochirurgicale de la Pitié de 1928 a 1950). *Sem. hôp.*, Paris, 1951, 27: 201.

Intrinsic stenoses of the aqueduct of Sylvius are rarer by far than the extrinsic types. The difficulties associated with determining their etiology, interpreting the histologic features, and finding an appropriate treatment for the resulting hydrocephalus render these cases a subject of special interest. Of the 19 cases here reported, only 13 were confirmed anatomically, and of these, clinical data were lacking in 4 cases. In the 6 purely clinical cases, ventriculographic findings and, in some instances, operative findings indicated a stenosis of the aqueduct. Three groups of cases are described, namely, the anatomically verified tumoral and nontumoral cases and the clinically observed cases. As regards age incidence, there were 4 patients up to 1 year of age, 2 patients from 1 to 10 years, 3 patients from 10 to 20 years, 9 patients from 20 to 40 years, and only 1 patient beyond 40 years of age.

Among the anatomically verified cases, in 8 the condition was due to tumors of the aqueduct, and in 6 to nontumoral stenosis; in 2 newborn infants, a congenital origin was certain, in another infant, probable, and in an adolescent the stenosis appeared to be due to a gliosis of unknown origin. Stenosis due to congenital malformation appears rare after the first year of life. In adolescents and adults symptoms recur at odd intervals, becoming progressively worse. In infants, it is often the increased size of the skull that draws attention to the condition.

Symptoms include subacute or chronic intracranial hypertension, a pyramidal syndrome, a cerebellar syndrome and, occasionally, a separate or associated infundibulohypophyseal syndrome. In infancy and early childhood hydrocephalus develops rapidly, and the increase in the size of the skull involves chiefly the frontoparietal region as contrasted with the slight expansion of the posterior fossa. Associated congenital malformations such as spina bifida and angioma are common.

The headache is almost constant, usually posterior, occasionally frontal or temporal, and varies in degree. It may regress spontaneously and in some cases it is accompanied by dizziness, vertigo, or psychic disturbances. Visual disturbances are common. Epileptic attacks, paraplegia, or even spasmodic quadriplegia, spontaneous vestibular disturbances, dwarfism, primary amenorrhea, retarded appearance of secondary sex characters, and genital impotence have been reported. Pedunculoprotuberantial symptoms are rare. All of these symptoms are dependent upon the hypertension and hydrocephalus caused by it, and usually disappear after operation.

Pneumoventriculography reveals a characteristic funnel-shaped image, or a triangle showing the initial portion of the aqueduct dilated above the obstacle. It may be difficult to exclude extrinsic stenosis due to tumor. Iodoventriculography may reveal the funnel image in cases in which pneumoventriculography fails. The two diagnostic methods, therefore, complement each other. The criteria for diagnosing tumoral as opposed to nontumoral cases are presented; however, differential diagnosis is often impossible.

The tumoral stenoses were usually due to the presence of small peri-ependymal glioma, histologically designated as glioblastoma in 3 cases, astrocytoastroblastoma in 2 cases, and astrocytoma in 3 cases. One of the latter tumors was calcified. Anatomic differentiation of these peri-ependymal tumors from the diffuse gliomas of the cerebral trunk is discussed. The latter rarely cause hydrocephalus except in the terminal stages and are manifested clinically by progressive focal symptoms.

In the 5 cases of nontumoral stenoses, only a single case showed evidence of an inflammatory lesion, namely, a peri-ependymitis or ependymitis superimposed on aplasia of the duct. Glial or neuroglial hyperplasia or pure gliosis are more often demonstrated. The various theories of etiology are reviewed. The congenital factor is recognized in all as supported by the frequent association of other congenital malformations.

These stenoses are more or less well tolerated according to the degree of the obstruction and the individual reaction. Mild exacerbations due to congestion or localized edema may precipitate ventricular retention even in cases of slight stenosis. Such conditions might also explain sudden attacks and remissions noted in the histories of adolescents and adults.

The treatment of intrinsic stenosis of the aqueduct of Sylvius consists in deobstruction by the direct or indirect method. Catheterization of the aqueduct (Dandy) has yielded successful results in some cases but is also dangerous, especially in the presence of possibly unsuspected tumor. Derivation of the cerebrospinal fluid may be accomplished by the opening of the supraoptic lamina, permitting access of the ventricular fluid to the chiasmatic cistern (Stookey and Scarff), or by Torkildsen's method of establishing communications between the ventricle and cisternus magnus by the introduction of a plastic tube. Good results lasting for years have been obtained with these two methods in nontumoral types of obstruction. The method of Stookey and Scarff does not always function as well as might be hoped, and

in cases of marked hydrocephalus the weight of the brain may be enough to close the orifice; also, the sudden escape of fluid following opening of the supraoptic lamina may lead to fatal cerebral collapse. This method should therefore be reserved for cases of moderate hydrocephalus. Torkildsen's method of derivation has yielded excellent results in both tumoral and nontumoral stenoses. Secondary obstruction due to arachnoiditis may develop after any type of operation. Derivation should always be combined with radiotherapy, owing to the uncertainty of the etiologic diagnosis and the relative frequency of tumoral stenoses.

In the present series, only 11 of the 19 patients were operated upon. In 4 cases, since tumor was suspected, an immediate operation by the posterior route was performed. One patient was subjected to a simple decompressive trephination in the first stage, and 6 years later the frontal cornua of the ventricle was opened without relief. He died 1 month later, in spite of a Torkildsen derivation operation. In another case of simple decompression followed by negative exploration, the patient survived 9 years. In 1 case of membranous stenosis treated by rupture of the membrane, the patient was reported well 4 years after operation. One patient treated by opening of the temporal cornua survived only 6 weeks. In an adolescent of 18 years, in whom symptoms had been present for 5 years, a Torkildsen derivation brought relief from symptoms; however, this case was followed up for only 3 weeks. In 2 cases treated by opening of the supraoptic lamina, 1 patient was reported in good condition 2 years and 3 months after the operation, whereas the other patient, although at first relieved of his symptoms, suffered a recurrence after 18 months.

These results would seem to justify the use of these two procedures for the treatment of hydrocephalus of various causes. In 4 cases, death was attributed to the use of pneumoventriculography in the presence of marked hydrocephalus; however, ventriculography is often indicated in spite of its danger, which is less than that of untimely intervention on the posterior fossa. In cases in which hydrocephalus is judged to be marked, from the thin layer traversed by the trocar, it is preferable to resort to iodoventriculography at once. EDITH SCHANCHE MOORE.

Treatment of Otogenous Temporal Lobe Abscess. HANS BRUNNER. *Ann. Otol. Rhinol.*, 1950, 59: 943.

The author makes an attempt to prove that brain abscesses of otogenous origin are more logically treated by the otologist at the time of surgery, through the mastoid and the tympanic cavity.

"The strictly neurosurgical methods may drain the abscess very well; yet they do not eliminate the primary source of infection of the ear and, thus, render two or more surgical procedures necessary in order to take care of the entire area of infection."

He also states that "even radical surgery upon the brain can be performed through an infected field without taking the risk of a spreading infection of the brain and the meninges." Although 35 cases of otogenous temporal lobe abscesses are reported, 4 of these were discovered at autopsy and hence were not included in the mortality rate. It is not stated whether or not these patients had surgery upon the ear without finding the abscess. Of the remaining 31 patients, 25 were treated by the "old method," with a mortality rate of 72 per cent. The so-called "old method" was not discussed. The "open method" of treatment was used in 6 cases with a death rate of 17 per cent.

The open method consists of a "cross incision of the dura, introduction of the cannula into the abscess, and marsupialization of the abscess." It is stressed, however, that under no circumstances should adhesions between the dura and arachnoid be torn.

"If, however, a cerebral abscess is associated with a marked brain edema, a primary and permanent herniation is to be expected if the open method is used. For this reason, the open method is not an ideal approach in the presence of brain edema; yet it is an excellent procedure to relieve rapidly a brain edema; consequently, it should be used—despite its drawbacks—in instances in which the brain edema menaces the life of the patient."

JACK I. WOOLF, M.D.

SPINAL CORD AND ITS COVERINGS

Laterally Placed Cervical Discs: A Review of 12 Cases. MICHAEL JEFFERSON. *Lancet*, Lond., 1951, 260: 129.

The author presents a study of 12 patients with cervical nerve root disturbances due to a ruptured cervical disc. In 4, the diagnosis was proved at operation and in 2 others, by myelography. The remaining 6 were those with a presumptive diagnosis on clinical grounds. The most frequent site was at C7 (7 cases), and the next most common site was at C6 (4 cases). Although one patient had a disc at D1, there was also a simultaneous compression by a second disc at C7. Lumbar puncture was performed in 11 patients and a normal pressure was found in all. Total protein was elevated in only 2 cases (65 and 70 mgm. per 100 ml.).

Although localization of the exact nerve root involved may be somewhat difficult in some cases, there is usually a fairly reliable distribution of the pain, which can establish the nerve root involved. The pain very seldom extends below the wrist, whereas sensory disturbances such as paresthesias are more severe in the hand and fingers. With involvement of the sixth cervical root, pain is referred to the anterolateral aspect of the upper arm and to the extensor aspect of the forearm. Paresthesias are most frequent in the thumb and index finger. A lesion of the seventh cervical root results in pain in the posterolateral aspect of the upper arm with paresthesia or numbness in the middle or index finger. Irritation of the first thoracic root gives pain in back of the upper arm, the ulnar side of the forearm, with

paresthesias in the little and ring fingers. Evidence of motor disturbances in the extremity is more difficult to ascertain since there is a frequent functional and self-protective mechanism.

X-rays of the cervical spine may be only of corroborative evidence if narrowing of the interspace and osteoarthritic changes correspond with the clinical level. It is realized that frequently the x-rays may be completely negative, whereas in other cases there may be more widespread evidence of osteoarthritis even in patients without symptoms.

The author makes a plea for conservative treatment. This consisted of complete immobilization of the neck by a plaster collar including the head and the upper chest, since it was felt that an extensive cast was necessary for complete immobilization. The plaster cast was usually worn for 6 to 8 weeks, after which partial immobilization could be maintained by a leather collar. Although he states that "in all cases so treated, pain and other symptoms were rapidly relieved," and "cure remained permanent on removal of the cast, except in one patient," it is not clear whether the patients who were operated upon also received this treatment without benefit. It must be presumed that conservative treatment was carried out in 8 patients and that since excellent results were obtained in all by the conservative treatment, it is still very worth while. In the one patient who had a recurrence of pain after the removal of the cast, ultimate relief was obtained by heat and graduated physical exercises. It is agreed that operation should be reserved for those whose symptoms are of long duration and who resist more modest courses of action. JACK I. WOOLF, M.D.

Compression Syndromes of the Cervical Nerve Roots; Contribution to the Differential Diagnosis in Arm Pains (Ueber Wurzelkompressionssyndrome bei Osteochondrose der Halswirbelsaule; Beitrag zur Differentialdiagnose der Brachialgien). H. J. UHLEMANN. *Deut. med. Wschr.*, 1951, 76: 37.

This article is based on the study of 50 ambulatory patients who were treated for arm pains at the Neurology Clinic of the University, in Hamburg-Eppendorf, by the author and co-workers. Uhlemann points out the fact that formerly, in most of these cases, the diagnosis of "plexus brachialis neuritis" would have been made, while now, with the help of x-ray examination, it is easy to demonstrate the existence of a pathologic condition of the spine, which is the etiologic factor for the pain syndrome.

In a great percentage of persons around the age of 40, the following pathological process will occur: destruction of the hyaline cartilage, overgrowth of the bones—osteophytes—loss of joint space, and sclerosis of the adjacent bones. In the cervical spine, the osseous protrusions form transverse ridges which encroach on the intervertebral foramina and compress the nerve roots. Sometimes there is a bulging, without rupture of the annulus fibrosus, or a rupture and complete or partial extrusion of the nucleus pulposus.

Although, as mentioned before, the occurrence of a degenerative arthritis is very frequent after the fourth decade, the number of occurrences of the painful arm is much less. There have to be additional causes in order to produce neuritic lesions in these subjects. The agents producing a mononeuritis or polyneuritis are multiple, as is well known; they may be toxic, infectious, or metabolic in their origin. In the cases reported by the author, the main clinical symptom was the pain. It was described in the different cases as tingling, burning, boring, stabbing, etc. In many cases it became worse at night and was aggravated by touching the affected area or by temperature changes. Frequently the pain was accompanied by more or less severe motor and vasomotor symptoms.

The treatment was directed against the acute neuritis-producing agent and, at the same time, against the predisposing chronic condition of the spine. Rest of the affected parts, salicylates, and other analgesics were usually helpful. Conservative orthopedic treatment was applied with success; the author found that the padded cardboard collar afforded a significant relief. He believes that surgical intervention should not be recommended until conservative treatment of the condition has been given a reasonable trial and has failed.

OLGA M. HARING, M.D.

Protrusion of Cervical Intervertebral Discs with Lesion of the Spinal Cord. RAGNAR MÜLLER. *Acta med. scand.*, 1951, 139: 86.

This article is limited to herniations of the cervical intervertebral disc resulting primarily in damage to the spinal cord, and is based on a study of 12 cases verified by laminectomy. That the recognition of this condition is increasing is found in the fact that although these 12 cases were collected from among admissions to the hospital during the period of 1940 to 1949, 6 of them were recognized only within the last year of this period. The difficulty of clinical diagnosis is confused by the mimicry of various degenerative diseases such as amyotrophic lateral sclerosis, progressive muscular atrophy, subacute combined degeneration, and multiple sclerosis. The author stresses the point that before making a definitive diagnosis of a degenerative disease, myelography should always be done.

Although 5 patients had signs of root pain at some period before their admission to the hospital, this had extended, in some cases, over a period of two decades. Only 2 patients gave a history suggestive of a traumatic onset. In nearly one-half of the cases there were no clinical signs of root compression. A study of the cerebrospinal fluid was completely negative in 9 cases and of no diagnostic significance in the others. Roentgenograms of the cervical spine showed spondylosis deformans of a variable degree, and were negative in only 1 case. Although this is not in general accord with some other reports in the literature, it is noted that these patients were all of older age and the condition had existed longer than

in many of the other patients whose cases were reported.

Air myelography was carried out in all cases and the findings were positive; however, in only 3 cases did a definite mass appear to be limited to one intervertebral disc, the others showing more extensive changes.

The results of surgery were not satisfactory since "in the majority of cases there was already irreversible injury of the spinal cord at the time of operation, as well as marked changes in the spine of the spondylosis deformans type." The author feels that surgery should be limited to decompression by laminectomy, with division of the dentate ligament in those cases with hard, bony spurs; however, if operations were performed before the discs have become calcified, the discs could be removed without damage to the cord. JACK I. WOOLF, M.D.

SYMPATHETIC NERVES

Lumbar Sympathectomy for Arteriosclerosis of the Lower Extremities. EDWARD A. EDWARDS and CHILTON CRANE. *N. England J. M.*, 1951, 244: 199.

The authors have carefully analyzed the results of lumbar sympathectomy for arteriosclerosis of the lower extremities in 100 consecutive cases. The majority of the patients were between 50 and 70 years of age. Diabetes was present in 27 cases. Despite the relative nonselectivity and the nature of the illness, there were only 2 deaths, one of these the result of a coronary thrombosis, and the other the result of hemiplegia and coronary thrombosis.

The postoperative complications of a more serious nature were pulmonary embolism in 6 patients, with recovery, pneumonitis in 1 patient, and atelectasis in another. Neuritic pain in the thigh occurred in about 50 per cent of the patients, although it was severe in only about 11. This pain usually started about the tenth postoperative day and continued for several weeks. Although 70 patients had threatened or actual necrosis, only 6 required thigh amputation following surgery.

There were only two definite contraindications to sympathectomy: (1) "visceral disease of such severity that the patient might be expected to succumb to the operation, and (2) deep necrosis proximal to a toe." Although marked hypertension and diabetes exerted a moderately unfavorable influence on the outcome, it was felt that the occasional good results made the procedure worth while. Preoperative paravertebral or spinal anesthetic blocks were believed to be of very little value. Of 30 patients so tested, all of whom obtained good results, 9 showed a poor response, 3 showed no response, and 1 patient had an actual fall in temperature.

This study suggests that the operation should certainly be more widely applied to the arteriosclerotic patient. The authors state that at this time we have no other form of therapy that approaches sympathectomy in its immediate and long effectiveness.

JACK I. WOOLF, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Tuberculosis of the Male Breast (La tubercolosi della mammella maschile). NICOLA ROSSI. *Arch. ital. chir.*, 1950, 73: 359.

Of all cases of mammary tuberculosis only 3.6 per cent occur in men. Factors accounting for the low incidence may include the absence of changes associated with pregnancy and with menstruation.

Two cases of mammary tuberculosis in the male are reported, on the basis of which the author cites the blood stream as the portal of entry. He comments on the marked inflammatory infiltration of the underlying pectoralis major muscle and the sclerotic reaction surrounding the foci which may dispose to the spontaneous arrest of the process.

EDITH B. FARNSWORTH, M.D.

Extensive Secondary Axillary Lymph Node Carcinoma without Clinical Evidence of a Primary Breast Lesion. HOWARD A. WEINBERGER and DEWITT STETTEN. *Surgery*, 1951, 29: 217.

The authors record the case histories of 5 patients in whom an involved axillary node was palpated as a solitary mass in the absence of clinical breast findings. In each instance, following excision of the axillary node, it proved to be a carcinoma metastasis, and after clinical elimination of the possibility of skin or lung or other distant primary lesion, the patient was immediately treated for an operable carcinoma of the breast by a classical radical mastectomy. Subsequent examination of each amputated breast demonstrated a small primary malignancy. It is the opinion of the author that this information provides a significant demonstration of the bahavior of a small group of carcinomas of the breast, and it is strongly suggested that carcinoma in an axillary node of a female, in the absence of a clinically detectable malignancy elsewhere in the body, particularly in the lung, should be treated without delay, as a metastatic deposit from a clinically undetectable primary breast lesion.

ORVILLE F. GRIMES, M.D.

Carcinoma of the Breast; Review of 206 Cases. R. L. SANDERS and R. M. POOL. *Am. J. Surg.*, 1951, 81: 193.

The authors present a statistical analysis of 206 cases of carcinoma of the breast in patients treated during a 13 year period. The ages of the patients varied from 26 to 84 years; 36 patients were less than 40 years of age, and 18 were over 65 years; 152 patients were between 40 and 65 years of age. The tumors had been present for periods ranging from 1 day to 25 years, and a greater number of patients presented a relatively short history of tumor in the latter half of the period studied than in the earlier years.

Of the 206 patients, 62 reported pain in the breast, but several others complained of a burning sensation, or of discomfort in the breast, or in the arm on that side. Many of these were early lesions, since 21 of the 62 had no metastases on microscopic examination of the resected specimen. Inspection and gentle palpation of the breasts in the supine, as well as in the erect position are important in the physical examination for carcinoma. Fifty-nine of the patients in this series had neither fixation of the breast to adjacent tissues nor palpable axillary glands. Needle aspiration is not advised, as it is believed that such a procedure is not only inadequate for diagnosis, but that dissemination of the tumor cells may occur. Biopsy of every breast lesion should be done before definitive treatment is instituted.

Radical mastectomy, according to these authors, is not contraindicated by axillary or supraclavicular metastases unless distant metastases are obvious. Ulceration is not a contraindication, nor should fixation to the chest wall be a deterring factor. Preliminary x-ray therapy is given in many advanced cases before operation.

When it is possible, radical mastectomy should be performed. If contraindicated, because of an extensive lesion, or because of the elderly age of the patient, x-ray therapy followed by simple mastectomy is suggested.

The two factors determining prognosis in carcinoma of the breast are (1) extent of the lesion, and (2) the grade of malignancy. The age of the patient appears inversely related to the prognosis. Mammary carcinoma arising during lactation offers a particularly poor prognosis. The location of breast tumors is important in that those situated medially will metastasize sooner to the mediastinum and lungs than those in the outer quadrants. Palpable axillary glands do not necessarily indicate metastatic involvement, since in this series only 21 per cent of those palpated were found to contain carcinoma. Conversely, 145 of the 206 patients had clinically negative axillas, yet 112 showed metastases when examined microscopically.

Of the 206 patients, 125 had definite metastases and 116 of these were subjected to radical mastectomy. Of the remaining 81, with only local growth, 72 underwent radical mastectomy. In the group undergoing radical operation, 115 were operated on at least 3 years previously and could be traced. Their survival is as follows:

Years of survival.....		3	5	10	15	20	25	Total
Without metastases.....	(37)	8	8	6	3	1	1	27(70%)
With metastases.	(78)	24	21	2	1	0	1	49(60%)
		115	32	29	8	4	1	2	76

No particular advantage was noted in comparing patients operated on since 1933 with those operated on previously.

The authors conclude that "a lump in the breast should be removed and examined under the microscope immediately upon its discovery and, if malignant, a radical resection should be performed. Until research brings us a better solution of the problem, we shall do well to adhere rigidly to this method of treatment. In so doing we may at least expect to reach a larger number of patients before the malignancy has spread and thus to increase to a material degree the number of our late survivals."

C. FREDERICK KITTLE, M.D.

Bases for the Integral Treatment of Cancer of the Breast (Bases para el tratamiento integral del cáncer de la mama). D. BRACHETTO-BRIAN. *An. Inst. med. exp.*, B. Air., 1949, 1: 49.

The author outlines a general plan for the treatment of breast cancer which has been used over a period of 2 years in managing more than 500 cases. A thorough endocrinologic evaluation and an investigation of liver function are undertaken and an attempt is made to correct deviations from normalcy. The classical Halsted operation is then the procedure of choice. No results from the follow-up studies in this series are as yet available.

THOMAS LANE STOKES, M.D.

Sarcomas of the Breast (Sarcomas conjunctivos de la mama en la mujer). D. BRACHETTO-BRIAN. *An. Inst. med. exp.*, B. Air., 1949, 1: 35.

Fourteen cases of sarcoma of the breast are reported, including 5 fibroblastic sarcomas, 1 reticulosarcoma, and 8 adenofibrosarcomas.

The author includes a section on the evolution and pathology of these neoplasms with several interesting photomicrographs. The clinical characteristics are well detailed to encourage early diagnosis.

The potentiality of cure is emphasized as all of these tumors except the reticulosarcoma have a low malignancy. The Halsted mastectomy and axillary dissection without roentgen therapy are recommended for fibroblastic sarcoma and adrenosarcoma. For reticulosarcoma x-ray treatment before and after mastectomy is advised.

THOMAS LANE STOKES, M.D.

The Rationale of Radical Mastectomy; a Review. DAVID H. SPRONG, JR., and WILLIAM F. POLLOCK. *Ann. Surg.*, 1951, 133: 330.

The author believes that there is a recurring tendency away from radical mastectomy as a treatment for breast cancer. The lymphatic drainage of the breast is primarily outward to the subareolar and subcuticular plexuses and thence to the regional nodes. Some of the literature pertaining to anatomy and therapy is reviewed. The principal route of extension is by the lymphatic channels to the regional lymph nodes. Mediastinal extensions frequently occur.

Skin removal should be in a radius of from 5 cm. to 9 cm. in every direction from the lesion. The flaps should be dissected to the sternum medially, the clavicle above, the latissimus dorsi laterally, and the rectus sheath below. The author pointed out that the cutaneous lymphatics and the subpapillary venous plexus are within a few millimeters of the skin, and therefore require a wide skin excision and a thin flap dissection. Both pectoral muscles should be removed completely. Axillary dissection should be complete; however, the long thoracic nerve and the thoracodorsal nerve are preserved unless involved in the tumor. It is believed that the careful, deliberate operator has a lower operative mortality rate, a lower recurrence rate, and twice as many living patients at the end of 5 years. The factors determining prognosis are not definitely known at the time of surgery, and can only be determined after pathological examination. The author repeats the criteria of operability pointed out by Haagensen and Stout. Evaluating and comparing different methods of treatment is difficult because of limited preoperative knowledge of the type of tumor and axillary involvement. He discusses the comparison of simple versus radical mastectomy.

There are two groups of factors which influence the prognosis. The first group is inherent in the patient. These factors are histologic grade of the tumor, location and size of the tumor, extent of involvement, age of the patient, etc. The second group of factors is entirely within the hands of the surgeon and includes: the amount of skin excised, the skin flap dissection, the complete removal of both pectoral muscles, the axillary dissection, the avoidance of operative trauma, and the consideration of radiation therapy. The value of radiation therapy is still to be determined as an adjunct to surgery. The author repeated that the radiation therapy is not a substitute for thorough dissection. Radical mastectomy should continue to be our standard treatment until better results can be proved for an alternative method.

ROBERT E. FLORER, M.D.

TRACHEA, LUNGS, AND PLEURA

The Effect of Lipiodol on Alveolar Gas Exchange. HARRISON BLACK and ALBERT ROOS. *J. Clin. Invest.*, 1951, 30: 338.

A study has been made of the pulmonary function in 10 patients, before and after bronchography by means of lipiodol. In only one patient was the alveolar-arterial oxygen pressure gradient found to be definitely increased following the procedure, although 5 patients, in addition to this one, showed an abnormally high gradient in the control study.

Arterial carbon dioxide tension was essentially uninfluenced by lipiodol. The vital capacity was reduced by an average of 7.6 per cent, several hours after bronchography. Measurement of the saturation time, on changing the inspired gas from room air to 100 per cent oxygen, revealed no significant effect

after the injection of lipiodol. Lung to ear circulation time was similarly unchanged.

All abnormal values returned to the control level within 24 hours, except in one patient in whom the prelipiodol values were not reached until 48 hours later.

The presence of lipiodol, therefore, has no significant effect on the respiratory gas exchange, except in occasional patients with advanced pulmonary disease. SAMUEL KAHN, M.D.

Thoughts on Lipoid Pneumonia and the Type of Oil Instilled by the Nasal Route; in Connection with an Observation of a Pulmonary Excision (Réflexions sur la pneumonie huileuse et le sort des huiles instillées par voie endo-nasale; a propos d'une observation d'exérèse pulmonaire). J. DELARUE, R. DEPIERRE, J. ROUJEAU, and J. PAILLAS. *J. fr. méd. chir. thorac.*, 1950, 4: 505.

The literature on the subject of fat in the lung is briefly reviewed, and the cases are classified into those of endogenous origin and those of exogenous origin.

The authors report the case of a 15 year old girl who, 20 days following a tonsillectomy, developed signs of suppuration of the right middle lobe of the lung. The patient became asymptomatic after treatment with penicillin. Radiologic signs persisted. After repeated bronchoscopic aspirations and biopsies, a pneumonectomy was performed 1½ years later. The specimen, which is described in considerable detail, consisted of a large cavity surrounded by dense, fibrous tissue and containing papillary projections in the lining which blocked the bronchi. Atelectasis and fibrosis were present in the surrounding lobes. There was much granulation tissue and much fat in the exudate. All lobes contained alveoli filled with lipophages.

In support of the belief that the fat was of endogenous origin is the fact that the common association of bronchial stenosis and suppurative bronchiectasis with localized fatty degeneration were present. The presence of a history of repeated instillation of nasal drops makes one equally certain of the exogenous origin of the fat.

The various types of oil (animal, vegetable, and mineral) causing pneumonia are briefly discussed. It is concluded that this patient showed a process probably containing fat from both sources. This could have been proved by physical, chemical, and histochemical techniques which were not used in this case.
THOMAS C. DOUGLASS, M.D.

Lung Cysts (Quistes aereos del pulmon). VICENTE N. ROGER. *Bol. Inst. clín. quir.*, B. Air., 1950, 26: 103.

This lengthy paper constitutes a running review of the opinions concerning lung cysts. Final arguments are to appear in a subsequent issue, but the present installment gives a breakdown of the experience on the services of J. ARCE and M. M. BREA.

Such general considerations as incidence, sex, age, and topographic distribution, theories of pathogenesis and pathologic anatomy, along with a historical review of the literature on the subject are presented.

The clinical picture, symptomatology, diagnosis, and differential diagnosis are elaborated upon. Treatment is discussed somewhat fully, emphasis being placed on surgical extirpation, but not neglecting an adequate preparatory regimen of postural drainage, antibiotics, and general supportive measures.

Twenty-seven patients have been operated upon since 1935. Of these, 21 have been cured, 1 was unimproved, and 5 have died. Obviously, the greatest mortality and morbidity occurred before 1942, during which period the tourniquet technique for resection was employed. Since 1942, the mortality rate has been only 9.5 per cent (2 of 21 patients), one patient having died of shock, the other from an asthmatoid state.

Among the postoperative complications encountered, there were 7 empyemas, 6 of which included a bronchial fistula. Shock occurred 5 times and asthmatoid states were recorded twice.

Lateral decubitus position for thoracotomy, using an intercostal incision, is recommended. Although enucleation of the cyst and partial lobectomy have been done, a total lobectomy is apparently preferred. Occasionally, of course, pneumonectomy may be required. The pleural space is drained, the bronchial stump is closed with linen, and pericostal sutures are used in closure. HIRAM T. LANGSTON, M.D.

Pneumonectomy with Replantation of the Lung in the Dog for Physiologic Study. ANDRE A. JUVENELLE, COLEMAN CITRET, CHARLES E. WILES, JR., and JOHN D. STEWART. *J. Thorac. Surg.*, 1951, 21: 111.

One successful replantation of a lung following pneumonectomy is reported. The operation was performed under endotracheal anesthesia and the Burns valve. The continuity of the pulmonary artery, the superior and inferior pulmonary veins, and of the primary bronchus was restored. The hilus was repleuralized. Vertification of the functional integrity of the lung was proved at operation, and later by clinical study. Pulsations of the pulmonary artery were felt beyond the line of the anastomosis. Fluoroscopic examinations revealed normal respiratory ventilation and aeration. By means of angiocardiograms the pulmonary artery and its branches were well demonstrated. Results of unilateral pulmonary ventilation studies have not as yet been reported. Deleterious effects due to section of the lymphatics were not observed.
BENJAMIN G. P. SHAFIROFF, M.D.

Surgical Treatment in 3 Cases of Pleural Sarcoma. SVEN RAMSTRÖM and HELGE HELLSTEN. *J. Thorac. Surg.*, 1951, 21: 116.

Three cases of localized benign mesothelioma are reported to have been discovered in middle-aged individuals on routine x-ray examination. On x-ray inspection, the tumors were well defined and attained a large size. Clinically, the tumors acted

in a benign manner but were capable of compressive manifestations. At operation they were easily enucleated. Microscopic sections were characteristic of fibrosarcoma with xanthomatous or myxomatous cells in varying concentration. Postoperative radiation therapy was given in each case.

BENJAMIN G. P. SHAFIROFF, M.D.

HEART AND PERICARDIUM

Situs Inversus of the Abdominal Viscera with Levocardia; Report of 8 Cases Submitted to the Blalock-Taussig Operation. MAURICE D. YOUNG and HERBERT E. GRISWOLD. *Circulation*, 1951, 3: 202.

Inversion of the abdominal viscera with levocardia is a rare anomaly in which the abdominal viscera are transposed, but the heart occupies its normal position in the left chest. A review of the literature revealed reports of a total of 14 cases.

Eight additional cases are presented by the authors. Angiocardiography and heart catheterizations were carried out in 6 cases and Blalock-Taussig operations then performed. An analysis of the cases reveals that (a) situs inversus of the abdominal viscera may be easily overlooked, (b) the mortality from operation is high, (c) inadequate pulmonary blood flow was demonstrated in every case, and (d) bizarre malformations of the aorta and its main branches, and also the venous return, are common.

W. FOSTER MONTGOMERY, M.D.

Treatment of Mitral Stenosis by Commissurotomy (Le traitement du rétrécissement mitral par commissurotomie). P. SOULIÉ, T. J. E. O'NEILL, M. SERVELLE, J. DI MATTEO, F. JOLY, J. CARLOTTI, and J. R. SICOT. *Bull. Soc. méd.* Paris, 1950, 66: 1665.

Two operations are at our disposal for the treatment of mitral stenosis: anastomosis between the pulmonary vein and the vena azygos, or creation of an interauricular communication. One more operation is still in the experimental stage, namely, arterial graft uniting the auricle with the left ventricle. A direct curative procedure is represented by valvulotomy.

The authors report 2 cases in which commissurotomy was performed. Both patients were women, one 24 and the other 21 years of age. Both recovered from the operation. Both patients had repeated crises of pulmonary edema, were totally incapacitated, and showed hemodynamic signs of impairment of the lesser circulation.

The operation was followed by a transient reaction of the left pleura and a reaction of the pericardium detectable in electrocardiograms. The typical diastolic murmur was replaced after the intervention by a simple presystolic impulse. The functional amelioration could not be evaluated because the patients were still resting at the time of the report.

Preoperative and postoperative catheterization of the heart showed in one patient a lowering of the systolic and diastolic pressure in the pulmonary artery after the operation but the mean pulmonary capillary pressure remained higher than the diastolic pressure. In the second patient the mean pulmonary capillary pressure and the diastolic pressure in the pulmonary artery, both equal before the intervention, were lower in equal measure after the operation.

Roentgenologic findings were not influenced by the procedure.

The operation is performed under endotracheal anesthesia. The section is carried chiefly through the external commissure. The authors stress the advisability of the operation in early stages of the disease.

JOSEPH K. NARAT, M.D.

Myocardial Ischemia and Its Surgical Relief. Review of 30 Cases. GEORGE A. MASON. *Lancet*, Lond., 1951, 260: 359.

The author presents a review of the case histories of 30 patients operated upon in an attempt to relieve myocardial insufficiency by surgical methods. The experience gained in the care of such patients over a 14 year period is presented.

The operative technique varied with the condition of the patient and the experience of the operator. In a patient whose general condition was extremely poor, an extrapleural cardiotomy (after removal of the seventh costal cartilage) was utilized, and either aleuronat paste was smeared over the pericardial sac or asbestos powder was insufflated into it. In the earlier cases, after transpleural exposure of the heart, a pedicled graft of greater omentum was applied to the heart.

Later in the series, the approach was somewhat changed. The third, fourth, and fifth left costal cartilages were removed and the pericardium was opened extrapleurally. The parietal pericardium was abraded with Beck's raspatory and was then either smeared with the aleuronat paste, or asbestos powder was insufflated into the pericardial sac; however, if the condition of the patient permitted, the omentum was first brought up either through the linea alba or in front of the medial part of the diaphragm, i. e., in front of, or behind the costal margin, and then brought into the pericardial sac deep to the intercostal bundles, spread over the heart surface, and sutured to the pericardium. For a considerable time, the omentum was not sutured directly to the heart, but it is the opinion of the author that this need no longer be feared.

Analysis of the statistics shows that 11 of the 30 patients operated upon did not survive the first month after surgery; 3 patients were not relieved of their angina symptoms; and 16 were thought to have been benefited by grafting, in 6 of whom relief is admittedly very problematical.

It must be remembered, however, that nearly all the patients were cardiac derelicts for whom there was very little, if any, alternative hope. To restore only a third of such patients to full activities, even temporarily, as well as to relieve them of their painful disability, seems to be worth while.

ORVILLE F. GRIMES, M.D.

Successful Repair of an Aortic Aneurysm with Sternal Perforation. R. ADAMS COWLEY, HERBERT E. SLOAN, and NEIL H. SULLENBERGER. *J. Thorac. Surg.*, 1951, 21: 159.

A female patient, 38 years old, was operated upon for an aortic aneurysm with sternal perforation. Preoperatively a mass was palpable just below the suprasternal notch. It was pulsatile and synchronous with the heart beat. The Kahn complement fixation test was positive for syphilis. Pain across the back and shoulders was the dominant complaint. Retrograde aortograms and angiocardiograms showed the ascending aorta to be markedly widened with no involvement of the innominate, carotid, or subclavian vessels. Other roentgenograms showed a perforation of the sternum.

At operation the aneurysm was found to arise from the anterior portion of the ascending aorta near its junction with the transverse arch. The left innominate vein was partially compressed, while the innominate artery was adherent to the aneurysm. The neck of the aneurysm was isolated and wrapped with strips of polythene film. After an uneventful postoperative course, the subcutaneous mass decreased in size and the texture of the overlying skin returned to normal. Ten months later, a considerable decrease in size of the superior mediastinal shadow was observed roentgenographically, healing of the sternal perforation occurred, and the patient had complete relief from pain.

BENJAMIN G. P. SHAFIROFF, M.D.

Revascularization of the Heart by Vein Graft from Aorta to Coronary Sinus. FERDINAND F. MCALLISTER, DAVID LEIGHNINGER, and CLAUDE S. BECK. *Ann. Surg.*, 1951, 133: 153.

The results obtained in experimental work on cardiac revascularization are presented. A vein graft, in several variations, was placed between the aorta and coronary sinus. An early problem was the regulation of flow into the sinus; neither a silk ligature nor a band of vein was satisfactory. Finally, the incision in the aorta was limited to 4.5 mm. longitudinally. A further problem was that of occlusion of the grafts. Dicumarol was used and abandoned. A simple over and over suture was finally decided upon. The graft was flushed with heparin and stored in saline until needed. The procedure of allowing a time interval between ligation of the sinus and application of the graft was abandoned.

Simultaneous ligation and graft resulted in a pooling of blood in the venous system, because of the limitation of the venous tree.

Subsequently the graft was placed without ligation, and ligation was performed later. This, of course, created a fistula, which condition was well tolerated. Ligation, later, was not satisfactory. After more extensive studies, the authors reached several conclusions: the stoma must be no larger than 4 mm. in diameter; the coronary sinus should not be completely ligated at any time; a fistula in the absence of ligation is well tolerated; if the coronary sinus at a second stage is partially occluded to 3 mm. in diameter, there is no further mortality, nor do the grafts become thrombosed. Furthermore, this two-stage procedure protected 12 out of 13 dog hearts against occlusion of the anterior descending branch of the left coronary artery.

ROBERT E. FLORER, M.D.

ESOPHAGUS AND MEDIASTINUM

Perforations and Ruptures of the Esophagus. JOHN M. DORSEY. *Surg. Clin. N. America*, 1951, 31: 117.

Acute suppurative mediastinits should be suspected in a patient with a previously normal temperature, pulse, and leucocyte count, who, upon endoscopy, develops shoulder, epigastric, or substernal pain, a temperature elevation of 1 to 2 degrees, and a white count of 11,000 to 25,000. Persistence of these signs is clinical confirmation. X-ray study with a radiopaque medium should be done to locate the defect, localize the mediastinal fluid, or demonstrate the presence of air. The author outlines the fascial planes of the neck with their respective extensions into the mediastinum. Five case reports are presented in detail.

1. Postendoscopy mediastinitis in a 54 year old male with a temperature of 104 degrees and a white count of 17,000, treated by 30,000 units of penicillin every hour, and hot compresses to a large crepitant left cervical mass.

2. Esophageal perforation treated by cervical mediastinotomy. The incision is usually made on the right if no localizing signs are present (as in this case). An incision overlying the anterior border of the sternocleidomastoid muscle can be used to drain abscesses as low as the fourth dorsal vertebra.

3. Postendoscopy mediastinal abscess, due to diverticulum and foreign body. The diagnosis was made on the finding of widening of the mediastinal shadows, a temperature 101 degrees, and the presence of mediastinal air. A cervical mediastinotomy was done and a Witzel gastrostomy to maintain nutrition. The diverticulum was excised later.

4. Mediastinotomy draining a suppurative mediastinitis with fatal results. A 26 year old female patient with lye ingestion stenosis suffered impaction of a meat bolus; 16 hours later she had a leucocyte count of 21,000 and a temperature elevation of 101 degrees. X-ray films showed extravasation of barium into the mediastinum. A gastrostomy and a posterior mediastinotomy were done, and the mediastinum was entered at about the eighth rib. A No. 16 Penrose drain was inserted. On the sixth postoperative day, one day after the removal of the drain, the patient died of profuse hemorrhage from the wound. Postmortem examination showed erosion of the aorta at the level of the eighth rib, and abscess formation at a point where the drain had been inserted. In retrospect, the authors would have done a transpleural mediastinal exploration, as in the following case.

5. A 57 year old male was seen 3 hours after impaction with a meat bolus. Following an unsuccessful attempt at removal, the patient's white count rose to 25,000 with a temperature of 103 degrees. The left chest was entered through the bed of the ninth rib; no site of perforation could be seen. Gastrostomy was done, with removal of part of the meat bolus; the remainder of the bolus was easily taken out by the endoscopist. Recovery was uneventful except for the development of tension pneumothorax on the fourth day.

The authors take this opportunity to present the good results they have obtained with the use of papain in the management of these cases. Papain is prepared from the fruit and leaves of the papaw tree and is capable of digesting 35 times its weight in lean meat. Combined with morphine and taken in small quantities at 15 minute intervals, it has been useful in relieving obstruction, and endoscopy in debilitated, older patients has been avoided.

JANE C. MACMILLAN, M.D.

Spontaneous Rupture of the Esophagus. DAVID DUNAVANT and EDWARD F. SKINNER. *Surgery*, 1951, 29: 527.

In 1947, the first case of recovery from spontaneous rupture of the esophagus was reported. The authors present 1 case in which cure was obtained by thoracotomy and drainage in conjunction with antibiotics instituted shortly after the rupture.

A 34 year old negro male was first seen complaining of pain in the left abdomen and chest following nausea and violent vomiting. Supraclavicular emphysema and a boardlike abdomen were noted on physical examination. Tenderness and rebound were most marked in the left upper quadrant. Bowel sounds were hypoactive. X-ray films revealed the emphysema, but were otherwise normal. The diagnosis was confirmed when a small amount of radiopaque oil, given orally, escaped into the lower mediastinum and left pleural space. A closed thoracotomy was performed. Gastric suction, antibiotics, and parenteral therapy was instituted.

The majority of cases of spontaneous rupture of the esophagus are seen in patients between 35 and 45 years of age who experience severe abdominal and chest pains during severe vomiting following heavy alcoholic consumption; a moderate degree of shock is usually present and the pain is constant; various degrees of dyspnea and cyanosis may be present; swallowing liquids or food causes severe pain in the chest. Subcutaneous emphysema may be palpable in the neck, or may be noted in the roentgenogram; it was present at some time in over 80 per cent of the reported cases. With the exception of trauma, no other condition, except possibly spontaneous pneumothorax, will produce mediastinal emphysema. The diagnosis may be confirmed by radiopaque oil, by mouth, and its demonstration in the chest film.

Generally, two types of operative treatment are advocated—thoracotomy with drainage and thoracotomy with repair of the laceration.

The time interval is an important factor in reducing the mortality. Esophageal tears should be closed if the diagnosis is made early. This is best done through transthoracic approach under endotracheal anesthesia. For patients in whom the diagnosis is made late, or who are critically ill, a rib resection and drainage of the pleural cavity with concomitant use of the antibiotics offers a better chance of recovery. Gastric suction and parenteral therapy is a necessity. Levine tube feedings can begin when the suction has been discontinued. The contralateral side of the chest should be watched for effusion, and drained if necessary.

HERBERT J. KAROL, M.D.

Partial Gastroesophagectomy for Esophageal Varices. GLENN E. SHELINE, DWIGHT E. CLARK, WILLIAM E. ADAMS, and DALLAS PHEMISTER. *Surg. Clin. N. America*, 1951, 31: 213.

About 5 per cent of hematemesis is attributable to hepatic cirrhosis or splenic anemia. Surgical treatment of portal hypertension due to intrahepatic obstruction is directed at controlling esophagogastric hemorrhage, hypersplenism, and ascites.

Splenectomy may be effective in relieving portal hypertension temporarily, but effects a cure only if the pathology is due to obstruction of the splenic vein. Intrahepatic portal hypertension is only slightly benefited by splenectomy.

Ligation of the coronary vein, with or without splenectomy, as well as transesophageal injection of the esophagogastric veins to relieve hemorrhage has proved disappointing. Some believe portal hypertension is increased by cutting down the collateral blood channels.

There have been encouraging reports about the results of portacaval shunts for the relief of portal hypertension. However, about one-third of patients who had gastrointestinal bleeding preoperatively had one or more episodes postoperatively.

Two cases in which bleeding was controlled by total gastrectomy in one and by gastroesophagectomy in the other are reviewed. To these are added 2 cases of partial esophagogastrectomy. The procedure was carried out through the left eighth interspace. The phrenic nerve was crushed, the pulmonary ligament divided, and the diaphragm opened radially. The spleen was removed, and the esophagus and stomach were mobilized. The lower 8 cm. of esophagus were resected to the cardioesophageal junction. The esophageal stump was then anastomosed to a new opening in the fundus of the stomach. The vagus nerves were divided.

In the second case the procedure was the same except that 3 cm. of the esophagus and 75 per cent of the proximal stomach were excised.

The results with gastroesophagectomy in the hands of other operators are reviewed. The follow-up period is too short for final evaluation, but the results in controlling gastrointestinal hemorrhage have been found to be very encouraging, and the mortality is not prohibitive.

ROBERT L. CRAIG, M.D.

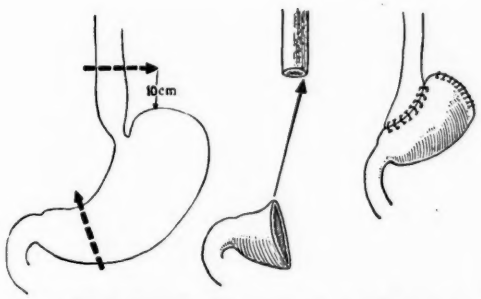

Fig. 1 (Womack *et al*). When resection is indicated, the acid-secreting portion of the stomach must be removed to prevent marginal ulceration. Note the method of esophageal anastomosis.

Benign Obstruction of the Lower Esophagus. NATHAN A. WOMACK, E. S. BRINTNALL, and J. L. EHRENHAFT. *J. Am. M. Ass.*, 1951, 145: 283.

A working classification of benign obstruction of the esophagus devised by the authors is based on anatomic and physiologic differences between the upper and lower portions of the esophagus. Striated muscle usually makes up the first portion, smooth muscle makes up the third portion, and the mid-portion is a mixture of the two types.

Classification of obstructions:

1. Paralysis or weakness of the striated muscle of the upper esophageal segment.
2. Failure of peristalsis in the lower esophageal segments from
   a. Hypothetical ganglionic degeneration
   b. Abnormal tonus of psychic origin
   c. Increased muscle tonus or contracture due to regurgitation of gastric juice or to ulcer
3. Abnormal local functionless contractions, seen most frequently in the aged.
4. Recovery or persistence of the primary cause with morphologic alterations such as
   a. Diffuse hypertrophy of the smooth muscle
   b. Esophagitis with or without ulceration
   c. Scarring

Most of the described cases fall into group 2. Studies of esophageal movement and theoretical explanations for the condition are discussed. The patients ranged between the ages of 12 and 79 years and males were more common than females. Dysphagia was the most common complaint, followed by weight loss, and regurgitated and retained esophageal contents. About one-half of the patients had retrosternal pain which was often disabling. Bleeding was occasionally noted. Almost one-third of the patients showed emotional instability, and one-fourth of them were psychoneurotic. All received a considerable amount of medical care before surgery was attempted.

Surgical procedures consisted of esophageal resection, vagotomy, esophagogastric resection, and esophagoplasty. When stenosis was noted, resection of the lower esophagus was done. It was determined that an extensive gastric resection must accompany esophageal resection to diminish acid secretion and marginal ulceration. The anastomotic line may require postoperative dilatation. The technique of surgery is outlined in Figure 1.

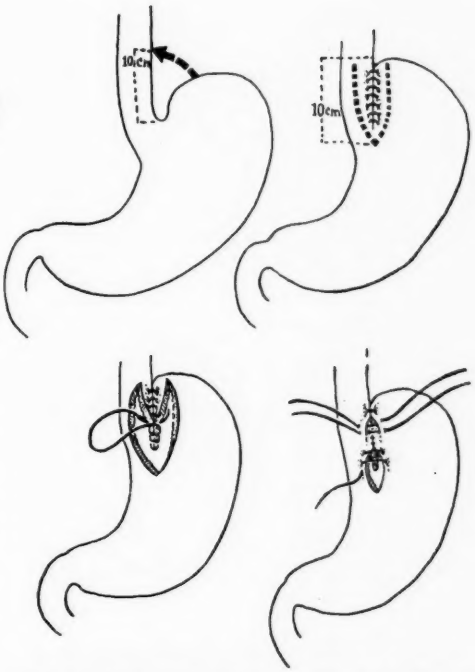

Fig. 2. This type of plastic repair makes it possible to interrupt all that portion of the circular musculature of the esophagus that may be involved in the obstructive process.

When feasible, an esophagoplasty is done. This is possible when peristalsis of the lower segment has failed and this is the main finding. The terminal esophagus must not be more than mildly inflamed. The technique is shown in Figure 2. Results have been excellent.

Regurgitation, ulceration, and excoriation of the esophageal epithelium is a major postsurgical problem. The techniques mentioned are attempts to relieve the patient and minimize the postoperative complications. ROBERT L. CRAIG, M.D.

Carcinoma of the Esophagus. CHARLES B. PUESTOW and JAMES H. CROSS. *Surg. Clin. N. America*, 1951, 31: 153.

The authors present 80 cases of carcinoma of the esophagus in patients seen at the Veterans' Hospital, Hines, Illinois. In 37 of these, the condition was operable. Dysphagia was the most consistent symp-

tom, anorexia was an early symptom, and weight loss and hematemesis were late symptoms.

Endoscopy, bronchoscopy, biopsy, and nutritional preparation of the patient are done preoperatively. Incision is made over the left seventh or eighth rib with removal of one entire rib, or two if needed; with retraction of the lung, the esophagus is exposed and mobilized. The resection line is made at least 5 cm. above the gross tumor of the lower third of the esophagus. The diaphragm is incised and the cardia of the stomach freed therefrom. The left gastric artery is approached posteriorly, and is clamped and divided close to its origin at the celiac axis. After mobilization of the stomach, a posterior row of sutures is placed through all layers so as to effect the gastro-esophageal anastomosis; then an incision is made through corresponding layers of the anterior wall of the stomach parallel to, and 6 to 7 cm. from, the suture line. A Rawson Abbott tube is placed well into the stomach; an anterior row of deeply placed sutures joins the cardia to the resected proximal edge of the esophagus; a small margin of omentum is used to protect the suture line; the diaphragm is closed and the stomach is anchored to the newly formed hiatus. One or two stab wounds for drainage of the chest are done, catheters are inserted, and the lung re-expanded, followed by a routine chest closure.

In lesions of the middle third of the esophagus, the progress of the operation is determined by the tumor relation to the aortic arch. Adherence may be due to invasion or inflammation. If the former is suspected, operation is abandoned; if the latter, blunt dissection mobilizes the entire esophagus. With incision of the pleura, esophageal resection is done above the level of the arch and anastomosis is made anterolateral to the arch. No attempt is made to close the mediastinum and the catheter drains are placed in the pleural cavity.

Lesions of the upper third of the esophagus require a combined cervical and transthoracic approach, located as they are, on a level above the aortic arch. The entire esophagus is mobilized up to and through the cervical incision. The stomach is mobilized, maintaining integrity of the right gastric and gastro-epiploic vessels, and anastomosis is made high in the neck, 4 cm. proximal to the tumor. The fundus of the stomach is anchored to the cervical muscles; a feeding and decompressing tube is inserted.

Postoperative problems are those of replacing blood loss, maintaining lung expansion, which is checked by daily roentgenograms, and antibiotics. Even with these measures, however, the mortality was about 33 per cent, largely because of the poor nutrional state of the patients. Only 4 of these 80 patients were seen early enough for operation and a probable cure. JANE C. MACMILLAN, M.D.

Management of Carcinoma of the Cervical Esophagus. DANELY P. SLAUGHTER and ERWIN H. ROESER. *Surg. Clin. N. America*, 1951, 31: 85.

Carcinoma of the cervical portion of the esophagus is less frequent than that of other parts of the organ. Until recent concepts of construction were developed, most attempts at treatment were made with irradiation and met with only occasional success. Surgical cure of cancer is more feasible in the cervical esophagus than in the thoracic portion because of the much wider lateral dissection and excision that can be accomplished in the neck. Tubular dissection is necessary for the excision of lesions in the thoracic esophagus.

As to the cause of carcinoma of the esophagus, it is reasoned that some of the various forms of chronic irritation, such as intraoral sepsis, smoking, thermal irritation, and syphilis, which may contribute to the development of new growths in the oral cavity, may also play a role in cancer of the cervical esophagus.

The early symptoms may be only a sense of throat irritation or slight discomfort in swallowing. Dysphagia is the most commonly associated symptom in carcinoma of the esophagus, but it is a late manifestation when the primary neoplasm is in the cervical esophagus. In this area the esophageal wall is thin, flexible, and devoid of sensory nerve fibers. To cause obstruction to the passage of food may require involvement of a considerable segment of the esophageal wall. Pain and discomfort in the neck are usually late manifestations.

The differential diagnosis includes foreign body injury to the mucosa, globus hystericus, Plummer-Vinson syndrome, thyroid disorders, cervical rib, lymph node hypertrophy, metastases, retropharyngeal abscess, contiguous esophageal tumors, paresis of the laryngeal muscles, and osteoarthritis of the cervical spine. Fluoroscopic study of the esophagus with a thick barium suspension should be carried out, and all irregularities of the mucosal pattern and intraluminal projections detected should be studied with direct esophagoscopy and biopsy of the suspicious changes in the epithelium.

X-ray therapy has not proved successful in the cure of carcinoma of the cervical esophagus. Although esophageal carcinoma is radiosensitive and curietherapy has yielded encouraging results in a few cases, the results for the most part are unsatisfactory or palliative.

The surgical attack on cervical esophageal carcinoma is designed for complete extirpation, with sacrifice of the contiguous cervical structures if necessary. The primary tumor may be widely resected in continuity with its regional lymphatic drainage with low mortality.

In general, four surgical techniques for the ablation of cervical carcinoma have developed. The simplest approach is esophagotomy with local resection and primary restoration of luminal continuity. This procedure offers only a minimal resection of the esophagus and has an occasional indication in instances of early tumor limited to the mucosa. The authors report an illustrative case of local resection of a pedunculated adenocarcinoma.

A second method is the surgical construction of an artificial esophagus by mobilization of parts of the alimentary tract. The stomach, colon, and jejunum

have been mobilized. The subcutaneous tunneling of the jejunum from the abdomen to the neck for a direct esophageal anastomosis of mucosa to mucosa has been the most satisfactory procedure. Limitations to the tunneling process are excessive fat in the mesentery, narrowness of the mesentery, and poor distribution of the arterial arcades. Complications have been narrowing of the stoma, ulceration, fistula, and late intestinal necrosis from retrograde thrombosis.

A third technique is local resection and primary repair by means of a rectangular cervical skin flap. Once the diseased tissue is removed, the skin flap is placed across the prevertebral space and sutured into position. The upper edge of the skin flap is sutured to the cut end of the pharynx and the lower edge to the esophagus. A lateral cleft is left which is closed at a second stage. A Levin tube is inserted transnasally into the stomach. The remaining raw surface is covered with a split-thickness skin graft. This seems to be the most practical procedure yet devised for the tumor site. It cannot be used when the site of the tumor is low in the neck near the thoracic inlet.

Cervical gastroesophagostomy is the fourth surgical approach. The stomach is mobilized sufficiently to effect an anastomosis above the level of the tumor. Problems of this procedure are bronchial secretions, pneumonia, and coughing. Tracheostomy and persistent tracheobronchial aspiration are usually necessary. A small or contracted stomach may not be mobilized sufficiently for a cervical anastomosis, and it is safest to take a preoperative roentgenogram of the stomach to determine its size. The blood supply of the esophagus is richer than believed, and moderate mobilization need not be feared.

Diaphragmatic motion should be arrested to prevent pull on the anastomosis and episodes of increased positive pressure on the stomach. A segment of the nerve is removed instead of merely being crushed with a hemostat. Catheter drainage of both the apex and the costophrenic angle assures adequate expansion of the lung and drainage.

JACOB T. BRADSHER, JR., M.D.

The Diagnosis and Treatment of Cardiospasm. JAMES M. FRITZ, DWIGHT E. CLARK, and WILLIAM E. ADAMS. *Surg. Clin. N. America*, 1951, 31: 173.

The authors present a comprehensive review of the theories of etiology, the symptoms and diagnosis, and the nonsurgical and surgical treatment of cardiospasm. The true etiology has not been established. The symptoms are principally pain (early), intermittent dysphagia which is not related to particle size, and, later in the course, regurgitation of esophageal contents when lying down. This regurgitation may result in aspiration of esophageal content with pneumonitis, bronchiectasis, or lung abscess.

Physical examination and routine laboratory studies are usually of little diagnostic value, but x-ray studies, including a barium swallow, reveal varying degrees of dilatation. This may take three common shapes: (a) fusiform, (b) flask-shaped, and (c) sigmoid.

Routine esophagoscopy is usually not necessary to establish the diagnosis and may be both difficult and tedious on account of the difficulty in properly cleaning out the enlarged esophagus. If there is marked S-shaped deformity, visualization of the cardia may be impossible.

More valuable diagnostically is the successful passing of a No. 60 French sound. This should be done over previously swallowed and anchored size D twisted silk.

Nonsurgical treatment suffices in the majority of cases. In 10 per cent of cases the diagnostic passing of a No. 60 sound will afford temporary relief of symptoms and half of these patients remain well. The majority, however, require more prolonged and thorough dilatation, and for this the majority of authors prefer the Plummer modification of the Russell hydrostatic dilator. This should be done over a previously swallowed thread and fluoroscopic control after this is not necessary, and may be more dangerous. Vinson reports that in a series of over 500 cases so treated, 75 per cent remained primarily well after a short course, that the others could usually be controlled by repeated dilatation, and that there have been no deaths among these patients in the past 23 years. The occasional patient who is not adequately benefited may require surgical aid.

Various dietary regimens, alone or in combination with such drugs as atropine, nitrites, or prostigmine have been used without much benefit.

The operations advocated for the relief of cardiospasm include: (a) partial excision of the esophageal wall; (b) esophagoplication; (c) phrenectomy; (d) vagectomy; (e) sympathectomy; (f) transgastric retrograde dilatation; (g) cardiectomy with reimplantation of the stomach; (h) longitudinal incision of the esophageal wall for several centimeters above, below, and through the narrowed site with transverse suture (Wendel adaptation of the Heineke-Mikulicz pyloroplasty); (i) side-to-side anastomosis of the dilated portion of the esophagus and fundus of the stomach, leaving a spur across the double opening thus created; (j) use of a spur-crushing clamp via gastrostomy; (k) esophagogastroplasty by the Gröndahl adaptation of the Finney gastroduodenostomy; (l) extramucous esophagocardiomyotomy (Heller adaptation of the Rammstedt pyloromyotomy for infantile pyloric stenosis). A single incision, fully 4 inches in length, is recommended.

Of these, h, k, and l are now in favor. Most American surgeons prefer the Gröndahl esophagogastrostomy, whereas the English surgeons use the Heller operation. Sweet favors the Wendel cardioplasty, but Barrett and Franklin report unsatisfactory results in late follow-ups. Reports on the Gröndahl esophagogastrostomy, which have extended for any distance into the postoperative period, display discouraging features. Some patients re-

main well; recurrence is observed in the majority of those followed up. If the anastomotic opening is a large one, peptic juice regurgitation may cause esophagitis, deep ulceration, and severe hemorrhage.

The authors state that reports in the literature indicate about 15 per cent of patients will be unrelieved by operation or will shortly thereafter have recurrent distress. They have made experiments with the Gröndahl type of esophagogastrostomy, on dogs, and state that large esophageal ulcerations developed in about 60 per cent of the animals. While vagotomy can cure these, in the dog, in one case of esophageal ulceration in a human, vagotomy did not prove successful.

Maingot, and also Barrett and Franklin report excellent results with the Heller operation. No American surgeon has reported a significant series of cases in which this operation was carried out. Those American surgeons who have done some Heller operations have been discouraged by the failure of patients to secure adequate relief from the primary difficulty. BEATTY H. RAMSEY, M.D.

MISCELLANEOUS

Esophageal Hiatus Hernia. WILLARD VAN HAZEL and ROBERT J. JENSIK. *Surg. Clin. N. America*, 1951, 31: 189.

Esophageal hiatus hernia is now accepted as the most common form of diaphragmatic herniation. The passage through the diaphragm of the esophageal tube favors its development. The passage is formed by a muscular ring, and both the pleura and the peritoneum are reflected from the tendinomuscular diaphragm upon the esophagus and stomach by the diaphragmaticoesophageal membrane. This is made of areolar fibrous and elastic tissue. The diaphragm undergoes constant movement with swallowing and respiration; repeated abdominal pressure along with the intrathoracic negative pressure are other natural factors. Many believe that the herniation is congenital, whereas others maintain that the constant interplay of the factors mentioned, and other factors on the opening produce an acquired herniation. The authors believe that trauma, by producing a tearing force leading to weakness, is not given due regard in the etiology of diaphragmatic herniation.

The most common symptom is epigastric distress, more particularly after the largest meal of the day, and more pronounced if the patient lies down immediately after the ingestion of a large meal. Nausea and vomiting may be present, and emptying of the stomach by emesis may give relief. Hematemesis indicates a complicating ulceration. Very large hernias, by occupying intrathoracic space and by changes in intrathoracic pressure, may result in dyspnea and palpitation. Unexplained anemia is not infrequent. Many patients may have no symptoms. There may be little relationship between the size of the hernia and the severity of the symptoms.

Occasionally, more than one x-ray study may be necessary to reveal the herniation. The prone position, right side, with the use of localized pressure, may be necessary. The authors have encountered patients who had been subjected to so much intra-abdominal pressure with a belt as to render the examination unreliable.

The authors do not believe that short esophagus should be included in the above condition.

They present 6 case reports illustrating variations in the symptom pattern, and the method of treatment. They use phrenemphraxis for temporary control in obstructive cases, and follow later with diaphragmatic repair, and also for cases complicated by other serious disease such as myocardial damage or coronary artery disease. Both transabdominal repair and transthoracic repairs are used.

BEATTY H. RAMSEY, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Torsion of the Great Omentum. H. A. Hashemian. *Brit. M. J.*, 1951, 2: 276.

Torsion of the great omentum is a well recognized condition, but the number of recorded cases is comparatively small. The torsion may be primary or secondary, complete or incomplete. Primary torsion, when there is no recognizable cause for it, is the less common. In secondary torsion, a hernia, neoplasm, omental cyst, tuberculosis, or evidence of past or present intraperitoneal inflammation is present.

The cause of torsion is still in doubt. A change in the relative position of the omentum from any cause, such as a sudden twist or fluctuations in intra-abdominal pressure, may produce kinking. The stasis in the tortuous veins, which ensues, favors the completion of the torsion. Finally, occlusion of the straight arteries occurs. It is said that the condition occurs more often in stout persons. Overloading or uneven distribution of fat in the omentum increases the tendency toward pedicle formation, and this, in turn, predisposes to torsion. The torsion usually presents itself in the right iliac fossa because the right side of the omentum is larger and more mobile. Violent body movements may predispose to torsion in some cases.

The preoperative diagnosis of torsion is seldom made. Most of the cases are diagnosed as appendicitis, although the patients look less toxic than patients with appendicitis. The age incidence is between 35 and 55 years. The condition is twice as common in males as in females.

Three cases are reported. Samuel Kahn, M.D.

Twenty-Three Cases of Omental Torsion. Kai Nielsen. *Acta chir. scand.*, 1950, 100: 545.

The author reviewed the pathology, symptomatology, and treatment of torsion of the omentum. His article is based on the literature and 23 of his own cases.

Because of the constantly increasing efficacy of surgical treatment of hernias, omental torsion tends to become less frequent. The symptomatology is variable and not characteristic, and therefore it is possible to make the proper diagnosis preoperatively in only a small number of cases, even though the surgeon directs his attention to the following symptoms, which may serve as a guide:

1. Pain and slight incarcerations from an existing hernia, if any, occurring in association with the onset of the disease.
2. A palpable mass.
3. A certain disproportion between the relatively slight subjective symptoms, the more or less unaffected general condition, and the remarkably severe local abdominal signs.

It is emphasized that in the treatment of this disease it is important, when omental torsion inside a hernial sac has been revealed, to make very certain of the condition of the intra-abdominal omentum, if necessary by means of herniolaparotomy.

Charles Baron, M. D.

The Repair of Pararectus Incisional Hernias by Posterior Transposition of the Anterior Rectus Sheath. LeRoy J. Kleinsasser. *Surgery*, 1951, 29: 97.

Occasionally, following the use of incisions about the rectus sheath, postoperative herniation will occur.

Anatomically, the weakest point is the area below the linea semicircularis where the posterior rectus sheath is deficient. The principal support is the intact transversalis fascia. Consequently, wide

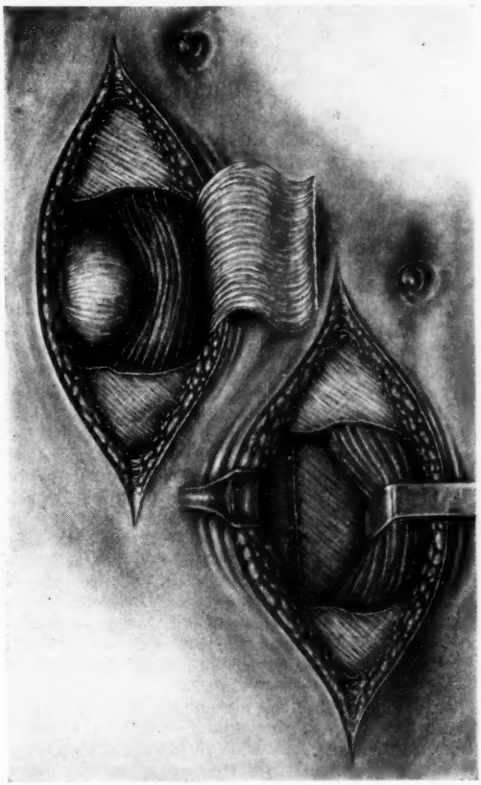

Fig. 1 (Kleinsasser).

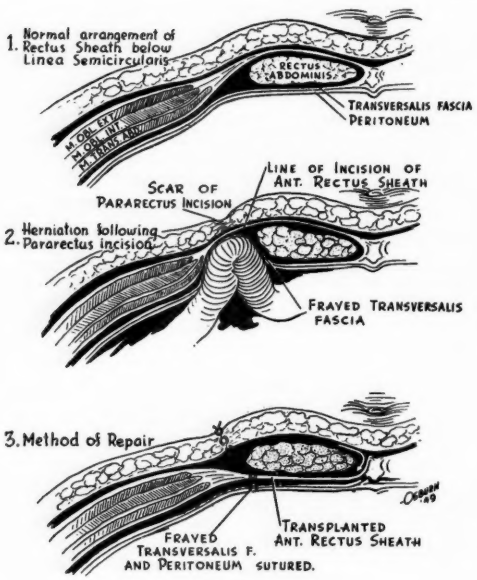
1. Normal arrangement of Rectus Sheath below Linea Semicircularis
RECTUS ABDOMINIS
TRANSVERSALIS FASCIA
PERITONEUM
LINE OF INCISION OF ANT. RECTUS SHEATH
SCAR OF PARARECTUS INCISION
2. Herniation following Pararectus incision
FRAYED TRANSVERSALIS FASCIA
3. Method of Repair
TRANSPLANTED ANT. RECTUS SHEATH
FRAYED TRANSVERSALIS F. AND PERITONEUM SUTURED.

Fig. 2 (Kleinsasser).

defects of this layer following operation or injury are prone to result in herniation.

The method of repair of incisional hernias about the rectus muscle that is being reported requires an intact anterior rectus sheath for practically its entire width (Figs. 1 and 2). The lateral edge of the anterior rectus sheath is incised well past the length of the hernia. The anterior sheath is then mobilized to the midline and the underlying rectus muscle is liberated. The anterior rectus fascia is then transposed beneath the rectus muscle and sutured laterally to the combined aponeurosis of the lateral abdominal muscles, and, above and below, to intact fascial layers. The peritoneal sac is treated as required. The repair is based upon the premise that an intact fascial layer is required just outside of the peritoneum for the prevention or repair of any peritoneal hernia. This appears especially necessary in the area below the linea semicircularis as the only effective support is the transversalis fascia, which becomes extremely attenuated in the presence of extensive hernias in this region.

Two cases in which this method of repair was used are reported in detail, the patients having been followed up for considerable periods of time without recurrence.

It is believed that this method is applicable to any defect of the posterior rectus sheath in which a sufficient width of anterior rectus sheath remains. A further application of this principle may be in spigelian hernia repair.

LEROY J. KLEINSASSER, M.D.

GASTROINTESTINAL TRACT

Corrosive Injury of the Stomach; Report of a Case Caused by Ingestion of Clorox and an Experimental Study of the Injurious Effects. DEMPSEY C. STRANGE, JOSEPH C. FINNERAN, HARRIS B. SHUMACKER, JR., and DONALD E. BOWMAN. *Arch. Surg.*, 1951, 62: 350.

Very few cases of corrosive injury to the stomach without involvement of the esophagus have been reported. In this case, a 49 year old man drank approximately a quart of clorox®, a commercial preparation containing 5.25 per cent sodium hypochlorite in water, with a *p*H of 10.8. Three months later he developed difficulty in swallowing, and any food ingested was promptly regurgitated. Roentgen rays showed a markedly constricted and shortened stomach, and a total gastrectomy was performed. The stomach measured 9 cm. from the cardia to the pylorus. Recovery was uneventful and the patient's condition was good 9 months after the operation.

Experimentally, the effect of clorox combined with certain body fluids on live rabbit skin was studied. Clorox when combined with saliva, gastric juice, or water proved to be very injurious to living tissue, while the combination of plasma with clorox appeared to provide some protection from injury. Other proteins, such as egg white and milk, provided a similar protection from clorox injury to the feet of a white rat immersed in various mixtures of these substances. This suggests the advisability of the ingestion of these foods in first aid following the drinking of clorox or similar solutions.

STANLEY W. TUELL, M.D.

The Relation of the Autonomic Nervous System to Gastric Secretion, with Particular Reference to the Sympathetic Nerves. PAUL W. SHAFER and C. FREDERICK KITTLE. *Surgery*, 1951, 29: 1.

The action of the sympathetic nerves on gastric secretion remains controversial despite numerous experiments, in contrast to the role of the vagus nerve, of which the effect is well established. In an attempt to delineate the function of the sympathetic nerves in gastric secretion, the authors constructed total gastric pouches after various procedures which altered the nerve supply of the stomach. Alimentary continuity was re-established by esophagojejunostomy. This type of pouch was prepared in 39 dogs. In 14, both the vagus and sympathetic nerves were left intact; in 12, bilateral vagotomy at the level of the cardia of the stomach was done while the pouch was prepared; in 9, bilateral transthoracic preganglionic sympathectomy with excision of the sympathetic chain and the splanchnic nerves from the region of the sixth thoracic to the second lumbar segments was done in a two stage procedure, which was completed approximately 2 weeks prior to construction of the gastric pouch; in 4 dogs, bilateral section of the cardioaortic and carotid sinus depressor nerves was done to create the generalized efferent sympathetic hyperactivity as described by Heymans. A minimum of 2 weeks was allowed to

lapse from the time of this procedure to the pouch operation. The efficacy of aortic depressor neurectomy can be established by the degree of secondary hypertension that it causes. In the authors' animals the mean systolic blood pressure following this operation varied between 180 and 240 mm. of mercury.

Each morning these animals were given 1,000 ml. of either normal saline or Ringer's solution intravenously, and following this infusion, a sample of gastric juice was collected for 60 minutes. The volume of gastric juice was measured and the samples analyzed for free acidity, *p*H and pepsin.

The results are listed below:

	c.c. / hr.	Free acidity	MCq. / hr.	*p*H	Pepsin c.c.	Peptic activity	Total peptic activity
Intact pouch (229)[1]	49	108	5.4	1.3	35	45	2,200
After vagotomy (182)	12	57	0.7	2.1	34	26	300
After sympathectomy (82)	76	110	9.0	1.5	38	43	3,300
After aortic neurectomy (45)	26	72	2.0	1.9	40	34	900

[1]Numbers in parentheses after various groups are total number of samples analyzed.

The authors conclude that following sympathectomy there is an increased volume of gastric juice and consequently a greater total acidity and peptic activity, which suggests that the sympathetic nerves normally inhibit gastric secretion. This correlates with the recent clinical reports of peptic ulcer formation and exacerbation following sympathectomy. Following vagotomy there is a marked dimunition in volume, acidity, and peptic activity. After aortic depressor neurectomy, the changes in the gastric secretion are similar to those after vagotomy, but not as marked in degree. C. F. KITTLE, M.D.

Acute Hemorrhage from Peptic Ulceration: An Analysis of 322 Cases. AUSTIN B. CHINN and ELDEN C. WECKESSER. *Ann. Int. M.*, 1951, 34: 339.

The incidence for acute hemorrhage in patients hospitalized for peptic ulcer ranges from 9 to 38 per cent. Despite the high incidence of the condition there is no universally accepted principle of management and its lowest possible mortality has not been clearly established. Records of 322 consecutive cases of proved peptic ulcer in which acute hemorrhage occurred either immediately before or during hospitalization in the University Hospitals of Cleveland have been closely examined with the belief that they may be helpful in the over-all planning of treatment.

The over-all mortality for the series is 13.3 per cent. A number of factors appeared to be related to the mortality, including age of the patient, site of the ulceration, duration of the ulcer, previous acute bleeding episodes, severity of the hemorrhage, bleeding after hospital admission, and serious complicating disease.

The most important single influence on the death rate was bleeding after hospital admission. In the medically treated cases the mortality among those that did not bleed after hospital admission was 1.2 per cent for duodenal ulcer and 3.2 per cent for gastric ulcer. The medical mortality of those that did bleed after hospital admission was 34 per cent for duodenal ulcer and 77 per cent for gastric ulcer. The surgical mortality for the patients operated upon to stop hemorrhage was 31 per cent for duodenal ulcer and 27 per cent for gastric ulcer.

Serious complicating diseases were present in 19 of the 28 patients who were treated medically and undoubtedly these diseases were a considerable contributing influence to the fatalities. Patients who show evidence of continued bleeding after hospitalization should be operated upon preferably during the first 24 to 48 hours. Patients who cease bleeding should be operated upon when there is evidence of recurrent hemorrhage. Gastric resection is the operation of choice, and the longer it is delayed the less its chance for success. The authors suggest an optimal program for the management of bleeding peptic ulcer which includes the following:

1. The patient is placed at complete bed rest, with adequate sedation to prevent restlessness.
2. The blood pressure and pulse rates are recorded at one-half hour intervals until stabilized at a normal level, then every hour for 48 hours.
3. The blood count, hematocrit, prothrombin time, and blood urea nitrogen are determined on admission, and the blood count and hematocrit are repeated at least every 24 hours. The patient is typed and crossmatched, and whole blood is made available.
4. Whole blood transfusions are started at the earliest possible time. In the first 24 hours, 1,000 ml. of blood are given, and each successive day 500 ml., until the red cell count is raised above 4 million.
5. If the patient is not vomiting and not in shock, oral feedings of a Sippy type are begun on admission; otherwise, effort is made to provide nutrition by the parenteral route.
6. Evidence of continued bleeding manifested by sustained hypotension and tachycardia, with or without hematemesis or bloody stools, is an indication for immediate operation. Recurrent bleeding manifested by a secondary drop in the blood pressure with tachycardia, with or without hematemesis or bloody stools, also indicates immediate operation.
7. Gastric resection with removal of the bleeding ulcer is the operation of choice. The stomach is opened to identify the bleeding point definitely. This operation is carried out with at least 2,000 ml. of blood readily available. In extreme cases this blood is administered by the intra-arterial route during operation; otherwise it is given intravenously.

HAROLD LAUFMAN, M.D.

Surgical Treatment of Bleeding Peptic Ulcers. WARREN H. COLE. *Surg. Clin. N. America*, 1951, 31: 271.

This article is concerned with the surgical management of peptic ulcer associated with hemorrhage.

The author first calls attention to the necessity for careful differential diagnosis of the lesion causing the bleeding. He states the two most common causes of hematemesis are peptic ulcer and esophageal varix.

Patients with mild hemorrhage from peptic ulcer may be treated conservatively, and if they do not respond they should then be treated surgically. Subtotal gastrectomy performed between hemorrhages is the method of choice.

Massive hemorrhage from peptic ulcer is a much different problem. The author advocates conservative care, with bedrest, gastric decompression, and transfusions. If the hemorrhage subsides in 6 to 10 hours, this therapy is continued and elective surgery is done later. If the hemorrhage persists beyond 10 hours, immediate surgery is performed.

The operative technique is discussed. The author stresses the importance of attacking the ulcer early in the operation in order to stop the bleeding. Ligation or transfixion of the bleeding vessel is advised. This may then be followed by gastric resection, with removal of about three-fourths of the stomach. The possibility of not finding the bleeding point in elective procedures is considered. The writer does not favor resection in this situation.

A case report is included, which illustrates some of the problems encountered in this disease.

DONALD C. GEIST, M.D.

At What Time Should the Surgical Intervention be Performed in Cases of Massive Hemorrhage from Gastroduodenal Ulceration? (Wann soll die operative Stillegung der massiven Blutung aus chronischen Magen-Duodenalgeschwueren vorgenommen werden?). FRANZ ROSE. *Deut. med. Wschr.*, 1951, 76: 41.

The author believes that the majority of patients with acute massive hemorrhage from gastroduodenal ulceration will benefit only temporarily from medical therapy. At the beginning of a sudden and large bleeding from peptic ulcer there is usually a fall in blood pressure and a reduction in the circulating blood volume. This drop in blood volume favors clot formation and consequently the cessation of bleeding.

Unfortunately, these natural mechanisms fail in most cases, and the hemorrhage continues or recurs within a shorter or longer time interval. Recurrent hemorrhage, or slow and continued bleeding are associated with a much higher mortality rate than the first massive hemorrhage. Based on his own experience, the author firmly believes that the most efficient method of conquering the attacks of bleeding is the application of radical surgery In his series of 17 consecutive cases, resection proved to be the treatment of choice.

The patient who has a massive hemorrhage with the classic picture of collapse should receive immediate and adequate medical treatment, including continuous and slow blood transfusions. He should be observed closely in respect of his hemoglobin rate, red blood cell count, blood pressure, pulse rate, and other manifestations of shock. As soon as the signs of severe shock have disappeared, and the hemoglobin level is not under 50 per cent, gastrectomy should be performed, as then the operative risks are best. This occurs usually within the first 18 hours after the hemorrhage has started.

OLGA M. HARING, M.D.

Changes in the Cephalic Phase of Secretion Following Gastric Resection in Ulcer. E. VELANDER. *Acta. chir. scand.*, 1951, 101: 49.

There is a rather common agreement that the erosive action of hydrochloric acid and pepsin on the gastric and duodenal mucosa is one of the most important factors in the pathogenesis of peptic ulcer. The stimulation of the cells to secretion is divided into the cephalic, gastric, and intestinal phases. The cephalic phase of gastric secretion is released by the vagus nerve. It was the general opinion that this phase was released by direct stimulation of the nervous impulses on the glands in the corpus of the stomach without action of a humoral factor such as is present in the gastric and intestinal phases. Uvnas, in 1942, showed experimentally in dogs that impulses from secretory fibers of the vagus released gastrin from the pyloric mucosa and that gastrin is the factor in releasing the gastric secretion. On the basis of these experiments it has been assumed that a similar mechanism initiates gastric secretion in the cephalic phase in man.

The author postulates, therefore, that a resection of the antrum in patients with peptic ulcer, because it removes most, and sometimes all, of the gastrin-producing cells, should abolish or essentially decrease the production of hydrochloric acid following chemical and also vagal stimulation. He investigates the effect of gastric resection upon the cephalic phase of secretion. Twenty-five patients with duodenal ulcer, 14 with gastric ulcer, and 2 with gastroduodenal ulcer comprise the series of cases. All had gastric resections of two-thirds of the stomach by the Billroth II method with retrocolic anastomosis, and all had a marked ulcer diathesis with prolonged periods of ulcer symptoms and a history of one or several complications. Ulcer symptoms were present from 1 to 30 years, with an average of 13 years. The postoperative results could be judged excellent in all but 2 patients. These 2 patients were able to work only part time 1 year after operation because of weakness, fatigability, and other complaints unrelated to their previous ulcer symptoms. One patient also had symptoms of gastric dumping, which responded to dietary management.

All of the cases were checked preoperatively and postoperatively for the quantity and acidity of the fasting secretion, and of the secretion following histamine stimulation and insulin stimulation. The histamine test gives an evaluation of the absolute value of free hydrochloric acid and therefore indicates the presence of glands producing hydrochloric acid. The insulin secretion test measures the cephalic phase of gastric secretion. The first postoperative

tests were carried out on the tenth day after resection, the second tests after 6 weeks, and the subsequent tests at intervals of 3 months.

Preoperatively, all of the patients with duodenal and gastroduodenal ulcer had pronounced hypersecretion of the fasting stomach, as well as after insulin and histamine stimulation. All of those with gastric ulcer had normal or subnormal secretion in these 3 phases of secretion.

Postoperatively, 100 per cent of the patients with gastric ulcer had a lasting anacidity in the fasting secretion as well as in the secretion during the cephalic phase and that after histamine stimulation. There was, likewise, a considerable reduction in the quantity of gastric juice secreted. A decrease in the quantity of secretion and in hydrochloric acid secretion was found immediately after resection, but a gradual increase to the final value occurred several months after operation.

In the patients with duodenal ulcer there was a significant decrease of secretion in all phases, but it was most marked in the cephalic phase. However, during the fasting secretion, achylia was eventually present in only 60 per cent, following insulin stimulation in 68 per cent, and following histamine stimulation in 56 per cent. The gastroduodenal ulcers were both achylic 6 weeks postoperatively.

The author believes that, as the acid-bearing cells were not anatomically completely removed in these cases, the drop in gastric secretion and acidity can be explained only by complete or almost complete removal of the gastric secretory cells of the antrum and pyloric regions. He believes that the greater drop in acidity after the insulin secretion test (representing the cephalic phase) as compared with the histamine test, further substantiates this opinion.

The postoperative decrease of acidity and secretion is ascribed to the following factors: (1) the removal of the main site of production of gastrin, the antrum, and hence a diminished production of this hormone; (2) reduction of the number of acid-producing glands; (3) more rapid emptying rate of the stomach remnant, which therefore is unable to make full use of its remaining secretory capacity during the gastric phase; (4) maximal neutralization of the free hydrochloric acid still present in various cases by an increased regurgitation of alkaline duodenal juice, and by the profuse occurrence of mucus; (5) a postoperative gastritis, believed due to the mechanical trauma caused by the resection, and irritation of the gastric mucosa by the backflow of alkaline duodenal juice; this gastritis gradually leads to atrophy of a large number of parietal cells. There is possibly also an atrophy of disuse in the cells due to the elimination of the gastrin stimulus.

FREDERICK C. HOEBEL, M.D.

Postgastrectomy Syndromes; A Study in Applied Physiology. CHARLES WELLS and RICHARD WELBOURN. *Brit. M. J.*, 1951, 2: 546.

The physiological effects of the various types of gastric resection are enumerated. These effects are described under four headings: rapid emptying of the gastric remnant, stasis and reflux, reduction of acid, and removal of the intrinsic factor.

These effects give rise to two groups of postgastrectomy syndromes: postprandial syndromes and deficiency syndromes.

The postprandial syndromes are further divided into early and late. Among the various types of early postprandial syndromes are the efferent loop dumping syndrome, postprandial diarrhea, afferent loop stasis and bilious regurgitation, afferent loop reflux, and gastric distention. The hypoglycemic syndrome is a late postprandial syndrome and is considered a consequence of rapid emptying.

The deficiency syndromes are described from the standpoint of loss of weight, including diminished caloric intake and impaired digestive absorption. Other deficiency syndromes are iron deficiency anemia, macrocytic anemia, and vitamin B deficiencies.

The management of each of these is discussed. The authors state that although a considerable proportion of patients have a disordered economy after gastrectomy for peptic ulcer, nearly all of them are well satisfied with the results of their operations. This report did not include a comparable analysis of vagotomized patients.

HAROLD LAUFMAN, M.D.

Intubation, Enterostomy, and Laparotomy; Their Place in the Treatment of Intestinal Obstruction. CHARLES GALE. *Med. J. Australia*, 1951, 1: 317.

Considerable difference of opinion exists as to the appropriate use of intubation suction decompression, enterostomy, and laparotomy in the treatment of the obstructed bowel. The correct viewpoint is that intubation suction, enterostomy, and laparotomy all have their place, to be used alone, successively, or in conjunction with one another, according to definite indications. Intubation suction used according to these indications has considerably decreased the necessity for enterostomy, and has rendered laparotomy unnecessary in some cases and technically easier in all cases in which it had to be performed.

For intubation, a short gastric or duodenal tube and a long intestinal tube are minimum requirements. When prolonged intubation suction is necessary, intestinal suction with a long tube has material advantages over decompression with a short tube: the decompression is more rapidly attained, oral feeding may be instituted as soon as the tip of the tube is beyond the duodenojejunal flexure, and subsequent laparotomy is made safer and easier. The presence of the tube allows ready identification of the proximal part of the bowel and direct decompression of the bowel suture lines.

In most cases of obstruction of the small bowel, intubation with a long tube with continuous suction should be started without delay; the necessity for operative treatment in addition depends, commonly in this order, on the presence of strangulation, the

failure of attainment of satisfactory decompression, the inability to maintain adequate nutrition, and the failure of the obstruction to resolve. Failure of attainment of decompression is due in most cases to the presence of a closed loop obstruction, which, if persistent, requires either enterostomy or direct release of the obstruction. Continuance of proximal intubation constitutes an essential part of the postoperative management.

In obstruction of the large bowel, intestinal intubation decompression may be worthy of trial in two types of cases: (1) when obstruction is early and colonic distention is slight, as suction may prevent further increase in colonic distention for a sufficient period to allow conservative measures to succeed in re-establishing colonic patency; and (2) when colonic obstruction is associated with an incompetent ileocecal valve, the cecal wall is hypertrophied, and the intraluminal pressure never becomes severe. Colonic decompression is thus not so urgently required. Considerable advantages are associated with successful decompression in these cases. The necessity for colostomy or cecostomy, which might prove a technical embarrassment to subsequent colectomy, is avoided, and if the tube is left in position during the preoperative preparation, it will provide useful decompression of the suture line of ileocolostomy after right colectomy, or of the small bowel after left colectomy.

With regard to intubation, intestinal obstructions may be divided into three groups:

1. Obstructions requiring early operation, intubation being used as an adjunct to treatment. This group includes strangulating obstructions of the small bowel and all obstructions of the large bowel.

2. Cases in which prolonged intubation is expected to result, in most cases in resolution of the obstruction. These are obstructions of the early postoperative period and those accompanying peritonitis.

3. The remaining nonstrangulating obstructions of the small bowel. In these, long tube suction is used with the knowledge that operation will be performed at the end of a variable period of time. It is used because of the striking contrast between the conditions found at such elective operation in the hydrated, nourished patient with decompressed bowel, and those found in the dehydrated, starved patient with abdominal distention who is subjected to immediate operation. This contrast is so striking that it is held that the advantages far outweigh the danger of overlooking a serious strangulation.

Details are given of the management of long tube intubation in obstruction, these including the passage of the tube, the determination of the passage through the pylorus, the changes occurring during migration of the tube and during the establishment of decompression, the phenomena associated with maintenance of established decompression, the criteria of resolution of the obstruction, the roentgenologic appearances at various stages, and the maintenance of hydration and nutrition throughout intubation. With these methods, it is apparent that if the tip of the tube comes to lie in the gastric fundus, it is apt to remain there for an inordinate period; but if it can be made, by various maneuvers, to lie in the prepylorus, it will pass through the pylorus and down to the most proximal block within a reasonable period.

A technique of intubation is described. Eleven cases, with 2 deaths, are reported, to illustrate the advantages, disadvantages, and technical details of intubation. SAMUEL KAHN, M.D.

Intussusception in Children Under 2 Years of Age; An Analysis of 54 Cases from Charity Hospital of Louisiana at New Orleans. H. REICHARD KAHLE. *Surgery*, 1951, 29: 182.

The mortality from intussusception in children under 2 years of age at the Charity Hospital of Louisiana, New Orleans, has fallen from 63.6 per cent in 1938 to 25.9 per cent in 1949. Delay before operation remains the chief reason for the high mortality in this condition, and it appears that physicians are as much to blame as are the parents. Postoperative obstruction occurred in 4 cases and is a possible explanation for the delayed mortality.

Since July, 1947, 10 patients with intussusception have been treated at the hospital with no deaths. The improvement is attributed to a sounder concept of pediatric surgery and to co-operation between the surgical and pediatric services. Five patients in this series obtained reduction from a therapeutic barium enema. HAROLD LAUFMAN, M.D.

Crohn's Disease and Intestinal Tuberculosis (Maladie de Crohn et tuberculose intestinale). GEORGES BROHÉE. *Acta gastroenter. belg.*, 1950, 13: 1091.

Crohn's disease is a circumscribed, chronic, benign, lymphogranulomatous reaction with a tendency to progressive hyperplasia of one or several segments of the digestive tract. The disease is a clinical but not a pathologic entity.

Seven theories of the etiology and pathogenesis of Crohn's disease have been advanced: *mechanical:* adherences, abnormal valves or foreign bodies such as talcum powder; *microbic:* Escherichia coli, streptococci, bovine tubercle bacilli, tuberculous ultravirus, and others; *vascular:* obliterating endarteritis or endophlebitis, or blockade of the lymph vessels; *nervous:* hypersensitive sympathetic system; *allergic; lymphogranulomatosis:* Hodgkin's disease, Boeck's disease or sarcoidosis; *physicochemical:* advanced by Chess, who maintains that the lesion is caused by ingestion of a material with piezoelectric properties.

Piezoelectricity is a term associated with certain crystals with an asymmetrical arrangement of their atoms within the molecules. Such crystals have the property of developing electricity on their surface.

Benign lymphogranulomatosis may be interpreted as a disease of adaptation of the reticuloendothelial system to repeated stress, provoked by foreign bodies with piezoelectric properties.

The same hypothesis is applicable to intestinal tuberculosis. Both conditions occur in all races, in both sexes, at all ages, in various social strata, in individuals with different eating habits, and in the same regions of the digestive tract. The conditions resemble each other in that they produce nodules with giant cells, reticuloendotheliosis, submucous and subserous edema, ulcerations, necrotic zones, pseudopolypoid formations, abscesses, perforations, internal and external fistulas.

Similar to regional ileitis, intestinal tuberculosis may be interpreted as a benign lymphogranulomatosis. Koch's bacilli produce a phospholipid responsible for the condition, while the infection plays a secondary role. Both conditions yield to medical treatment in the early stages, and require surgical interference in advanced stages. JOSEPH K. NARAT, M.D.

Regional Ileitis and Pseudoileitis (Iléite régionale et pseudoiléites). L. DE CALUWE and M. FORNHOFF. *Acta gastroenter. belg.*, 1950, 13: 1118.

Ninety per cent of cases of regional ileitis occur in individuals from 10 to 40 years of age, and in 50 per cent of this group the condition occurs in the third decade. It occurs with equal frequency in both sexes, and usually in the last 50 cm. of the ileum. While accumulation of pus is rare, inflammatory masses and spontaneous or postoperative fistulas dominate the picture.

The authors are inclined to believe that the primary lesion is located in the lymphatic network of the involved segment, while the allergic reaction is of a secondary character.

At present ileotransverse colostomy with or without transection of the ileum above the stoma is the most popular surgical procedure. Conservative therapy is indicated only if the patient refuses operation.

In 3 cases observed by the authors the clinical picture was strongly suggestive of regional ileitis and yet exploration failed to reveal any pathologic condition. JOSEPH K. NARAT, M.D.

The Relation of the Factor of Growth to the Pathogenesis of Megacolon, Megaileum, and Megaduodenum. BLAKE FAWCETT. *Surgery*, 1951, 29: 491.

Several years ago, Swenson and his associates presented a new concept of the pathogenesis of megacolon in children. They produced evidence that a malfunctioning and partially obstructing segment of the rectosigmoid is responsible for the proximal dilatation of the colon. They demonstrated that with removal of this segment the proximal colon returned to normal size.

The author presents a case in which a similar dilatation of the proximal colon occurred following a perianal abscess with stricture in a child who had had a pull-through operation for imperforate anus. This dilatation did not exist when the child had a colostomy prior to the pull-through procedure, nor shortly after the pull-through was performed. Dilatation of the markedly narrowed rectum following the abscess produced some improvement in the colon. Interest in the subject brought to the author's attention a very similar case with imperforate anus, a markedly dilated ileum in 2 cases with partial obstruction of the terminal ileum, and marked dilatation and hypertrophy of the duodenum in 2 cases in which there was distal narrowing of the bowel.

Observation of the fact that in children partial obstruction of the colon produced extreme dilatation, while in adults it produced only hypertrophy, led to the belief that growth was a factor in the difference. To test this supposition, newborn puppies and adult dogs were operated upon and a partially obstructing band of polyethylene was wrapped around the sigmoid colon and secured with silk sutures. In the adults the band was tight enough to reduce the lumen to 30 per cent of the normal and in the puppies it was just snug around the bowel so that it would not constrict until the size of the bowel increased with growth of the dog.

In the 9 adult dogs that survived 3 to 4 months, the colons were dilated from 1.5 to 1.7 times the normal size, but hypertrophy was the major response. Only the puppies that lived 6 weeks had time to develop chronic obstruction and all of these had marked dilatation of the proximal colon. Those puppies living less than 6 weeks had no obstruction and consequently no dilatation.

FREDERICK C. HOEBEL, M.D.

The Pathologic Physiology of Congenital Megacolon. ROBERT B. HIATT. *Ann. Surg.*, 1951, 133: 313.

Congenital megacolon has been known as a clinical entity since its classical description by Hirschsprung in 1881. Many theories have been propounded as to its etiology, but none have been proved. The author, using motility studies, suggests that congenital megacolon is a disease in which the underlying defect is a disorganization of the peristaltic reflex in the rectum, the lower sigmoid, or in both, and in which there is a delicate balance between obstruction and the compensatory mechanism for overcoming the obstruction, i.e., hypertrophy and dilatation.

Three general groups of congenital megacolon resulting from variations in the pathologic picture are discussed. In the author's experience the most common type is that in which the hypertrophied and dilated portion of the colon ends abruptly just above the rectosigmoid junction. A second type, much less common but more difficult to treat surgically, is that in which the transition is more gradual. In a third form, also relatively rare, there is megarectum as well as megacolon.

Congenital megacolon is a dangerous disease. Death in the newborn is occassionally seen when obstruction causes perforation of the sigmoid before the compensatory mechanism of hypertrophy and dilatation can become established. Perforation in an older infant is rare. The author believes that enemas are one of the greatest sources of danger to

these patients. The patients often go into a state of shock following an enema, which he believes is due to water intoxication.

ELY ELLIOTT LAZARUS, M.D.

Hirschsprung's Disease. MARTIN BODIAN, C. O. CARTER, and B. C. H. WARD. *Lancet*, Lond., 1951, 260: 302.

The literature is briefly reviewed on the familial incidence of Hirschsprung's disease. The authors then report the genetic implications of 40 consecutive cases. Some of the cases in siblings and in twins are reported in detail. Brothers were found to be affected in a ratio of 1 to 8; none of the sisters in these cases were affected.

The authors then studied the results of rectosigmoidectomy. Three of the patients died—2 under anesthesia and 1 from peritonitis. The results otherwise were satisfactory.

The absence of ganglion cells in the involved segment is believed to be a pathogenic-pathologic finding. The involved segment varies tremendously in length, but in 90 per cent of the reported cases the condition occurred in the rectosigmoid. Much longer involved segments have been reported.

The authors report in detail a single case of agenesis of the intramural plexus and absence of nerve fibers. THOMAS C. DOUGLASS, M.D.

The Surgical Treatment of Congenital Megacolon. ROBERT B. HIATT. *Ann. Surg.*, 1951, 133: 321.

Since considerable evidence has been recorded to show that the abnormal physiology of congenital megacolon consists primarily of a lack of propulsive action of the rectum or of the rectum and the lower sigmoid, the logical method of cure is removal of the distal nonpropulsive segment. Little may be expected from drug therapy, lumbar sympathectomy, or partial resection. The author advises removal of the entire distal nonpropulsive segment.

A modification of the operative procedure devised by Swenson is described. Briefly, the operation consists of surgical intussusception of the entire rectum and the lower two-thirds of the sigmoid in one stage without proximal decompression. A detailed description of the procedure, well illustrated, is given in the original article.

ELY ELLIOTT LAZARUS, M.D.

Retrorectal Tumors. RAYMOND J. JACKMAN, P. LEMON CLARK, III, and NEWTON D. SMITH. *J. Am. M. Ass.*, 1951, 145: 956.

Extrarectal masses occurring in the presacral or retrorectal region are considerably more common than is indicated in the literature. The common idea that these tumors are rare is explained by the fact that most authors writing on the subject confine their discussion to the congenital or anomalous group, failing to take note of the inflammatory and neoplastic varieties. Since a great variety of lesions may occur in this region and since many of them are asymptomatic, they are discovered only on routine digital examination of the rectum and the examiner may be at a loss as to how to treat them. In making a differential diagnosis, as well as in treating them, it may be necessary to call on the neurologist, neurosurgeon, roentgenologist, and orthopedist, each of whom should know his limitations in dealing with them. These tumors are of interest to the proctologist from the standpoint of differential diagnosis and because some of them, particularly the dermoids, are not uncommonly manifested as perianal sinuses and are therefore confused with anorectal fistulas. In many instances histopathologic examination of excised tissue is necessary before a definitive diagnosis can be made.

The authors reviewed the records of all patients with a sacral, presacral, or retrorectal mass which was manifested objectively as an extrarectal mass on the posterior rectal wall. The study covered a 14 year period, from 1935 through 1948, and concerned all patients with retrorectal tumors. During this 14 year period there were 114 patients with palpable retrorectal tumors. In general, these tumors fell into two main groups: (1) indeterminate tumors for which no tissue was available for diagnosis, and (2) determinate tumors for which tissue was available. In 32 (28 per cent) of the 114 patients no tissue was removed, so that a definitive diagnosis could not be made. There were 17 males and 15 females. It was with the group of 82 patients who came to operation and from whom tissue was available for pathologic study that the authors were primarily concerned. There were 39 females and 43 males. The tumors were classified into five main categories: (1) inflammatory, (2) congenital, (3) neurogenic, (4) osseous, and (5) miscellaneous.

The 82 patients with determinate tumors were about equally distributed between the sexes. However, certain specific types of tumors had a sex and age predilection; for example, chordomas tended to occur in male adults, while teratomas and meningoceles were more common in female infants and children. For the group as a whole, the chief symptoms were backache, pain in the leg, and dysfunction of the bladder and bowel, with low backache as the most common symptom. Other symptoms consisted of rectal pain, constipation, paresthesias, and difficulty in walking. Hemorrhoidectomy had been done on 5 patients during the course of their symptoms from the presacral tumor; 3 of these patients had chordomas, 1 had a dermoid, and 1 had a neurofibroma. This again serves to emphasize the importance of digital and proctoscopic examination. A digital examination of the rectum is an especially important diagnostic procedure for patients complaining of low back pain. In the authors' series, proctoscopic examination ruled out the rectum as an etiologic site for the primary tumor, and in the case of inflammatory and dermoid tumors it was an aid in the definitive diagnosis.

Roentgenologic study of the pelvis was probably the most helpful single diagnostic procedure in the attempt to separate these tumors into three groups:

1. Tumors arising from the sacral canal, the most common of which are the ependymomas, which cause erosion of the canal by expansion and pressure. The margins of the bone were sharp and well defined. Neurofibromas may produce a similar picture.

2. Tumors arising from the sacral body itself, which are commonly characterized by a picture of expansion of the sacrum by an infiltrative process.

3. Tumors arising from structures adjacent to the sacrum, such as the teratomas that produce a picture of anterior sacral erosion and appear as extrinsic masses which may contain teeth or bone.

However, in most instances a definitive diagnosis could be made only after histopathologic study of the tissue. Patients with retrorectal masses should be questioned about injection treatments for hemorrhoids, and in the presence of a recurrent anorectal fistula which has been operated upon often, an infected presacral dermoid should be considered as a possibility.

The prognosis for patients who have inflammatory and congenital tumors, aside from chordomas, is quite good. Of the neurogenic tumors, the neurofibromas and neurilemmomas respond well to treatment. For the group of retrorectal tumors as a whole, the prognosis was favorable in about 50 per cent and poor in the remainder.

Carcinoid Tumors of the Rectum. R. M. SHEPARD, JR., L. H. STRUG, and J. H. DILEO. *Surgery*, 1951, 29: 205.

Two cases of carcinoid tumors of the rectum are presented. The preoperative biopsy in each case was diagnosed as carcinoma. Abdominoperineal resection was done in both instances. Performance of this operation is defended by the authors on the basis that in some instances carcinoid tumors have been known to metastasize. The authors believe that single submucosal nodules 1 cm. or less in diameter should be removed by local excision, and if microscopic study shows extension beyond the area of resection or if the nodule has extended to the external coat of the rectum, excision of the rectum should be done. Submucosal nodules greater than 1 cm. in diameter, and lesions which are ulcerating, infiltrating, or multiple should be removed by excision of the rectum. If there seems to be no extension beyond the rectal wall, sphincter-saving operations may be considered. HAROLD LAUFMAN, M.D

Imperforate Anus and Rectourethral Fistula in a 27 Year Old Man; Report of a Case. J. JAMES DUFFY. *J. Am. M. Ass.*, 1951, 145: 545.

Imperforate anus occurs once in every 6,000 to 10,000 births. Imperforate anus with rectourethral or rectovesical fistula is even more rare and when it occurs, unless relieved early, results in early death from pyelonephritis. The case reported in this paper is of particular interest as there existed an imperforate anus with rectourethral fistula which had not had definitive surgery until the age of 27 years.

At birth imperforate anus was recognized. The doctor made a blind stab wound in the perineum which successfully established a fistulous drainage of the rectal segment. This continued to drain if stools remained watery, until 5 years of age. There was occasional fecal drainage from the urethra. At 5 the child ate nuts, washers, and other indigestible objects, and developed a complete bowel obstruction. He was operated upon and a double barreled colostomy was done.

He remained well until 12 years of age when it was necessary to use anesthesia to remove impacted feces from the distal blind-end loop of bowel. The perineal stab wound had closed. Pyuria, urinary frequency, and nocturia persisted.

The colostomy remained a problem to the growing boy and prevented him from engaging in athletics, swimming, and association with other boys because he was constantly conscious of the odor and was troubled by unheralded bowel movements. Later, ambitions to have dates and marry were also prevented.

In 1949 a severe urinary tract infection sent him back to a urologist who, in course of x-ray examinations, demonstrated for the first time the location of the fistulous tract. Further x-ray studies were made of the colon, proximal and distal to the colostomy, and an operative approach to the problem was planned.

The first stage was a perineal approach to the rectourethral fistula. The fistula was closed, but further operative procedure was precluded at this time because of a drop in the blood pressure. Incapacity for erection followed this procedure but the fistula remained closed. However, the urine still contained 1 to 200 pus cells per high-powered field.

The second procedure was carried out about 1 month after the first operation. The colostomy stomas were inverted and the skin sutured over them. This area was isolated from the abdominal laparotomy wound. The abdomen was opened. The distal segment of the colon was thin-walled but not as short as was feared from the x-rays. The bowel was divided from the colostomy and after freeing proximal and distal loops an end-to-end anastomosis was done. The appendix and also the colostomy site were removed. The abdomen was closed without drainage. The patient was then placed in lithotomy position. The scar of the old fistulous opening was dilated until mucosa of the bowel was reached. An elliptical incision was then made around the opening. The coccyx was removed. The lower limb of the bowel was freed and brought down to a normal position for an anus and sutured to the skin edges without tension. The levator ani muscles approximated easily. The presacral space was drained and a large vented petrolatum pack, much larger than the eventual size of the anus, was placed in the anal opening. The immediate postoperative course was uneventful and the wounds healed per primam.

One year later, the results from the surgical standpoint are satisfactory. The anus admits the little

finger easily, the patient has full bowel movements without discomfort and can control bowel movements and flatus. He goes to the toilet electively and does not need to wear a pad. Capacity for erections has returned. Bladder capacity has increased. He lives a full, normal life.

FREDERICK C. HOEBEL, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

The Use of the Secretin Test in the Diagnosis of Biliary Tract Disease. A Report of 327 Case Studies. DAVID A. DREILING and JOAN J. LIPSAY. *Gastroenterology*, 1951, 17: 242.

The authors studied the biliary flow obtained by duodenal drainage following the intravenous administration of secretin. From the data of the tests performed on 327 patients with and without biliary tract disease, the authors described, quantitatively, the biliary pigment response to the secretin test.

There are fundamentally 4 types of responses, which are correlated very closely with the roentgenographic and laboratory findings. In patients with gall bladder function (Type A), the duodenal biliary pigment concentration (icterus index) drops to below 5 during the secretin test. In patients with no gall bladder function due to primary gall bladder disease or following cholecystectomy (Type B), the duodenal biliary pigment concentration (icterus index) does not drop below 10 during the secretin test. In complete obstructive jaundice (Type D) bile is absent from the duodenum throughout the secretin test. The fourth response (Type C) is fundamentally a Type A response occurring in patients from whom the gall bladder has been removed. It signifies partial obstruction of the common duct.

The authors believe that the secretin test for biliary function both complements and supplements the Graham test. It is particularly valuable for patients who have had their gall bladders removed and patients with jaundice from whom information concerning the patency and the precise localization of obstructions in the extrahepatic biliary tract can be deduced.

ROBERT TURELL, M.D.

Use of Radioactive Tracer Material in the Differential Diagnosis of Experimental Jaundice. WALTER W. CARROLL, ARTHUR S. BIDDLE, and JOHN A. D. COOPER. *Q. Bull. Northwest. Univ. M. School*, 1951, 25: 13.

Radioactive tetraiodophenolphthalein was administered intravenously to 12 normal dogs, to 11 dogs in which the common bile duct had been completely obstructed by ligature, and to 11 dogs in which acute liver damage had been produced by chloroform intoxication. Blood level determinations and renal and fecal excretion studies were made at frequent intervals for periods up to 48 hours after a single dose.

In the normal dogs the dye was removed rapidly from the blood stream during the first 6 hours, whereas animals with hepatocellular and obstructive jaundice showed retention of the dye for 24 hours or longer. In the normal dogs an average of 5.3 per cent of the injected dye appeared in the urine within 48 hours after injection, whereas in animals with hepatocellular and obstructive jaundice the averages were 14.6 and 44.1 per cent, respectively.

In the normal dogs, an average of 61 per cent of the injected dye was recovered in the feces, whereas the average recovery in the feces of the dogs with hepatocellular and obstructive jaundice was 6.4 and 33 per cent, respectively, of the amount injected.

These radioactive dye studies served to differentiate between hepatocellular and obstructive jaundice. The authors believe that the data obtained from the investigation warrant trial of the method in human subjects for the differential diagnosis of jaundice.

FREDERICK W. PRESTON, M.D.

Cystogastrostomy: A Treatment of Pancreatic Pseudocysts. FREDERICK H. BRANDENBURG, STEPHEN MADDOCK, and ROBERT J. SCHWEITZER. *Ann. Surg.*, 1951, 133: 219.

This article is a case report of a pancreatic pseudocyst treated successfully by cystogastrostomy at the Boston City Hospital. The preoperative diagnosis was subacute recurrent pancreatitis with biliary tract disease. At laparotomy a cystic mass, 8 by 10 cm., was felt posterior to the distal two-thirds of the stomach. Firm vascular adhesions had completely obliterated the lesser omental bursa, and the lesser curvature of the stomach was adherent to the left lobe of the liver. The anterior wall of the distal stomach was incised. The cyst was attached to the posterior stomach wall. An incision 3 cm. in length made into the posterior wall emptied the cyst contents into the stomach. Eight months after the operation the patient remained asymptomatic.

Accepted forms of treatment of pancreatic cysts are reviewed critically.

1. External drainage by marsupialization may be followed by persistent fistula, excoriation of the skin, and infection.

2. Excision of the cyst is usually regarded as the treatment of choice for true pancreatic cysts. However, this procedure is not always technically feasible and may be accompanied by many hazards. It is recommended for true cysts because 10 per cent of all pancreatic cysts are malignant.

3. Partial pancreatectomy is for selected cases.

4. The authors collected 24 cases of pancreatic cysts treated by cystogastrostomy from the literature. It is a relatively simple procedure technically and avoids the external loss of pancreatic enzymes and electrolytes. Because of the danger of malignant degeneration in proliferative cysts, this procedure is recommended only for pseudocysts.

In the reviewed cases as well as the present report, reflux of the stomach contents into the cyst could not be demonstrated roentgenographically. Such reflux has been mentioned as an objection to cystogastrostomy and appears to be theoretical rather than real.

CURTIS ARTZ, M.D.

Cancer of the Pancreas; A Clinical and Pathologic Study. L. THAMSEN, N. HJORTH, A. RØRGÅRD CHRISTENSEN, and M. BJØRNEBOE. *Acta med. scand.*, 1950, 139: 28.

The authors have analyzed all cases of cancer of the pancreas in which autopsies were performed at the Pathological Institute of the Kommunehospital, in Copenhagen, during the years 1935 to 1948, in an attempt to throw light on the early symptoms of this disease. There were 112 cases in all, 15 of which were excluded because they revealed secondary rather than primary tumors of the pancreas. Cancer of the pancreas appeared in less than 1 per cent of all autopsied cases at this institution. It represented 4 per cent of all autopsied cases of cancer in Copenhagen and Frederiksberg during the period from 1942 to 1944.

Cancer of the pancreas was found to be more common in men than in women (a ratio of 1.9 to 1) and was most frequent in the age groups from 60 to 70 years.

The tumor was in the head of the pancreas in 50 per cent of the patients; in the body or tail in 19 per cent; and involved the entire gland in 31 per cent. Metastasis developed in about 75 per cent of the cases, being more frequent in body and tail tumors than in head tumors. Twenty-six per cent of patients died without metastases. Glandular or mixed types were the most common histologically. Dilatation of the bile ducts was observed in 52 per cent of the cases. The disease was combined with other proved forms of cancer in 5 cases.

The duration of the disease is short; half of the patients in this group died in the first 3 months. Pain in the upper abdomen is the most constant symptom, and in 57 per cent of the cases was the first symptom; it increases in intensity at night. Jaundice is a frequent sign, but often occurs late in the disease, and is usually associated with pain; painless jaundice was much less common in the present series. Cachexia (loss of weight, anorexia, fatigue) appeared frequently and early and was often great. Occult gastrointestinal bleeding was of frequent occurrence. Uncharacteristic dyspepsia, intractable constipation, and diarrhea were less common symptoms.

Palpable liver was found in a small number of cases. The authors state that Courvoisier's law was of only slight importance in the diagnosis of cancer of the pancreas. Tumor was rarely present and ascites was not common; thromboses were not frequently observed.

Clinical laboratory tests offered little information in this group of cases. Roentgenographic evidence of changes in the stomach and duodenum aids in the diagnosis of cancer of the head of the pancreas.

A correct diagnosis was made while the patient was still alive in 30 per cent of the cases; an incorrect diagnosis was made in 70 per cent of the patients. Only 15 per cent of the cases were diagnosed correctly without operation. The present study did not offer much which would be of aid in the early diagnosis of this disease, but further use of tests for pancreatic enzymes in the blood and duodenal contents, x-ray examination, and glucose tolerance tests may aid considerably. DONALD C. GEIST, M.D.

One Hundred Cases of Carcinoma of the Pancreas; A Clinical and Roentgenologic Analysis. THOMAS RAY BROADBENT and HERBERT D. KERMAN. *Gastroenterology*, 1951, 17: 163.

One hundred and two cases of primary carcinoma of the pancreas were seen by the authors. Of these, 72 were located in the head and 30 in the body of the gland. The average age of the patients was 58.2 years. There was a ratio of 1.85 males to 1 female among the patients. There were 3.3 white patients to 1 colored patient. A lesion in the body of the pancreas produced symptoms for an average of 30.1 weeks, and a lesion in the head of the pancreas did so for 7.34 weeks. There was an average duration of 7.5 months before hospitalization. Numerous tables show the clinical and laboratory findings.

Completely negative roentgen findings were observed in 13 cases, although in 53.9 per cent of the total group a definite diagnosis of carcinoma of the pancreas was made. Mucosal changes of the stomach and widening of the duodenal loop were present in 21.7 per cent and 13 per cent, respectively. Eight of 102 patients had tumors which were resected, 7 of these being in the head of the pancreas. Eight patients were subjected to autopsy without surgical intervention, and the findings of 13 were described at operation. Fifty-two patients were subjected to biopsy and 20 of these were given palliative treatment by intestinal biliary anastomosis. An additional 21 patients were given palliative treatment, but not subjected to biopsy. The liver was enlarged in 50 per cent, and a primary mass was palpated in 46.1 per cent. Forty-five per cent of the patients had a marked weight loss and 43 per cent had abdominal tenderness. RICHARD J. BENNETT, JR., M.D.

MISCELLANEOUS

Left High Thoracophrenolaparotomy. Technique. Indications in Surgery of the Thoracic Esophagus (La thoraco-phréno-laparotomie gauche haute. Technique. Indications dans la chirurgie de l'oesophage thoracique). J. C. RUDLER. *J. chir.*, Par., 1951, 67: 233.

Access to the subaortic region of the thoracic portion of the esophagus can be obtained through (1) an incision over the left seventh or eighth rib, (2) a combined route, namely, a separate median or paramedian supraumbilical, and left thoracic incision, or (3) a classical low left thoracophrenolaparotomy.

Great difficulties are encountered when the abdominal organs and the middle or the upper portion of the esophagus must be exposed. Resection of the sixth rib with section of the adjoining ribs does not provide a satisfactory exposure of the stomach and the jejunum. Double incisions, such as those through the fifth and the eighth ribs, damage large muscular

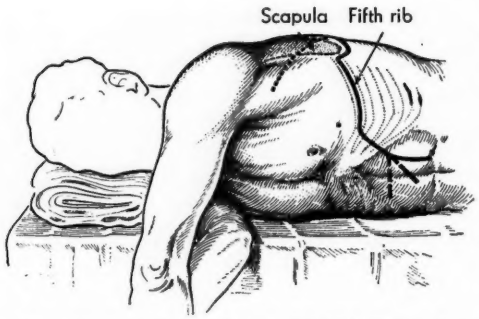

Fig. 1 (Rudler). Skin incision for left high thoracophrenolaparotomy.

areas with resulting shock. Gastrolysis through the abdominal route, followed by right thoracotomy, requires change of the patient's position and does not furnish a satisfactory exposure of the esophageal hiatus of the diaphragm.

The author recommends left high thoracophrenolaparotomy. The skin incision starts at the posterior angle of the fourth rib in the interscapulovertebral space, is carried around the tip of the scapula, follows the fourth rib to the chondrocostal articulation, crosses the anterior end of the fourth interspace, the fifth cartilage, the fifth interspace, the sixth rib, the sixth interspace, and reaches the costal arch over the seventh cartilage. From there it may be extended to the epigastrium in vertical, oblique, or transverse direction. The incision is 50 cm. long. The patient lies on his right side and the surgeon stands in front of him.

This method is suitable for excision of cancer of the supraaortic portion of the esophagus as well as for palliative supra-aortic esophagogastric anastomosis. For this purpose either the fourth or the fifth rib is resected, and the fifth, sixth, and seventh costal cartilages are sectioned. For total gastrectomy the left eighth or ninth rib is resected, and for low esophagectomy the sixth or the seventh rib is removed. The author employed this incision on 15 patients.

It is imperative to take roentgenograms of the chest the evening of the operative day in order to detect pneumothorax and to take care of it.

JOSEPH K. NARAT, M.D.

GYNECOLOGY

UTERUS

Carcinoma of the Cervix Uteri in an Infant. M. D. Baber, E. ap I. Rosser, and J. D. O'D. Lavertine. *Brit. M. J.*, 1951, 2: 392.

After a review of the literature, the authors present a case of cervical carcinoma in a child 15 months old. Abdominal section revealed fixation of the uterus to the bladder and hysterectomy could not be performed.

Postmortem examination revealed the cervix uteri to be greatly enlarged by a mass of hard white growth, 6.25 by 5 by 4.1 cm., which was friable and extensively ulcerated at the lower end. The body of the uterus was perched on the top of the growth, but the tubes and ovaries seemed to be normal. The bladder was adherent to the front of the mass, drawn up, elongated, and somewhat hypertrophied. Most striking of all was the enormous enlargement of the liver (weight 1,550 gm.) due to the presence of large numbers of secondary deposits, many of which were cystic and found to contain mucoid material.

Histologically, the primary growth showed a poorly differentiated adenocarcinoma with more solid cellular areas. The liver metastases showed a well differentiated papillary adenocarcinoma, in some places showing intimate mixing with the invaded tissues. The primary growth and invaded tissues were very closely intermingled, which factor was responsible for the original impression that the biopsy material represented a mixed tumor.

Charles Baron, M.D.

Considerations Derived from More Than 500 Diathermy Coagulations of the Uterine Cervix (Considerazioni su oltre 500 diatermocoagulazioni della portio). F. Bentivoglio. *Minerva gin.*, Tor., 1950, 2: 463.

Of the 508 patients treated by diathermy coagulation, 311 could be followed for more or less lengthy intervals following the operation. Of these 311 patients, in only 8 was it necessary to repeat the treatment, and in only 1 were more than 2 treatments required (3 coagulations—one in 1943, a second in 1945, and the third in 1949). This patient is now 41 years old and perfectly well.

The author uses the bipolar method and considers it perfectly satisfactory for an operator with sufficient experience. A milliamperemeter is intercalated to avoid overdosage (not above 400 to 500 milliamperes); however, except for intracervical work, the eye of the experienced operator is a sufficient guide to the amount of current needed. All treatments are ambulatory, with general or local anesthesia. Bed rest is advised for 1 day following the application of the method. The author has not seen any complications or bad results from the procedure.

Of special interest are the questions of subsequent pregnancies and of the possibility of dystocias. Thirty-three of these patients visited the department for consultation concerning a primary sterility; 26 of these could be subsequently followed. Three were found to be suffering from an endocervicitis exclusively, 9 from an exocervicitis, and 14 from associated endocervicitis and exocervicitis. The sterility had lasted from about 3 years to a maximum of 15 years. Following the coagulation, 7 of these patients became pregnant within periods varying from 3 to 6 months, 4 more became pregnant within a year, and 2 within 2 years. These 13 patients have now passed through 23 pregnancies, 2 of which ended as abortions; 14 delivered spontaneously; forceps were applied 6 times (in 4 cases at the level of the perineum and in 2 in the midportion of the pelvic tract); and there was 1 podalic extraction. In all these patients the dilatation was complete, or almost complete; in every case the indication for the interference was either fetal suffering or uterine inertia.

The author therefore believes that the objections to diathermy coagulation of the uterine cervix on the basis of postoperative complications (hemorrhages, lighting up of quiescent adnexal infections, etc.) are not justified, when the method of treatment is properly carried out, and for the proper indications.

John W. Brennan, M.D.

Total Abdominal and Vaginal Hysterectomy, a Comparison. Michael L. Leventhal and Maurice L. Lazarus. *Am. J. Obst.*, 1951, 61: 289.

This survey evaluates the morbidity in total abdominal and vaginal hysterectomy performed by the same group of operators for relatively comparable types of uterine disease. Thus 300 consecutive cases of total abdominal hysterectomy and 300 consecutive cases of vaginal hysterectomy, performed at the Michael Reese Hospital, Chicago, since January 1, 1946, were analyzed. Only private patients operated upon by the attending staff were considered.

These 600 operations were done by 15 surgeons. Among the senior men of this group, the number of abdominal and vaginal operations was about equal, while the men with less practice and experience choose the abdominal hysterectomy three times more often than the vaginal hysterectomy.

Very few nonparous women were subjected to the vaginal operation (5 in 300), which was done more often than the abdominal hysterectomy in patients in the fifth to seventh decades during which uterine prolapse is more common. Of the 300 patients operated on vaginally, 215 had reparative surgery in addition to the hysterectomy.

In both groups, fibromyomas were the chief indication for operation. In deciding whether the uterus should be removed abdominally or vaginally,

the determining factors were the presence of adnexal disease, previous surgery, size of the uterus, fixation, relaxations, and carcinoma.

The usual definition of morbidity was applied, namely, a temperature of 100.4°F. (38°C.) on any 2 postoperative days except the first 24 hours. When the uterus was removed alone, without any additional surgery, the morbidity was 24.5 per cent in the abdominal cases and 38.1 per cent in the vaginal cases. If also one or both of the adnexa were removed (without plastic procedures for the vaginal cases), the morbidity was 27.9 per cent in the abdominal, and 40.1 per cent in the vaginal, hysterectomies. When vaginal hysterectomy was combined with the removal of the adnexa plus plastic operations, the morbidity rose to 52.5 per cent. Previous surgery did not seem to affect the morbidity in either group. As to the various causes of morbidity, the incidence of urinary retention and urinary tract infection was higher after vaginal hysterectomy, while respiratory infections, paralytic ileus, venous thrombosis, pulmonary embolus, and ureteral injury appeared more frequently after abdominal hysterectomy. The only death in the entire series occurred 8 days after an abdominal hysterectomy and was due to pulmonary embolus. In both groups, patients subjected to spinal anesthesia had a somewhat lower morbidity than those who had general anesthesia. Spinal anesthesia did not cause a greater incidence of urinary retention than general anesthesia.

It is interesting that one of the senior surgeons, who does not use parenteral fluids routinely, had a comparatively lower incidence of urinary retention. This, he contends, is caused by overdistention of the bladder, which is likely to occur when an excess of fluids is administered during and after the operation, because the bladder is less sensitive to the nerve reflexes after use of the anesthetic drugs.

The over-all morbidity was greater after vaginal, than after abdominal, hysterectomy. However, the more serious postoperative complications occurred more often after abdominal hysterectomy. The average length of hospital stay was the same in both groups. HERBERT TEICHNER, M.D.

Morbidity After Total Abdominal Hysterectomy. JOSEPH HYDE PRATT, MADISON J. LEE, JR., WALTER F. HASSKARL, JR., and ROBERT W. BRANDES. *Am. J. Obst.*, 1951, 61: 407.

A program was set up by the authors to evaluate some of the factors affecting postoperative morbidity. Total abdominal hysterectomy was the operation chosen, since it is one of the most commonly employed gynecologic techniques and is done often enough to facilitate statistical analysis of the different steps. The study of 3 series of cases was undertaken to determine the effect on surgical morbidity of (1) preoperative vaginal preparation on the operating table, (2) intraperitoneal sulfathiazole, and (3) simultaneous appendectomy of patients undergoing total abdominal hysterectomy.

The 3 series consisted of comparable groups of cases of total abdominal hysterectomy and the findings should be significant, since no known factors except preparation of the vagina, intraperitoneal use of the sulfonamides, and earlier ambulation influenced the results.

As a result of their study the authors concluded that vaginal preparation with soap and water and antiseptic in the operating room before operation is an important factor in lowering the surgical morbidity after total abdominal hysterectomy.

Also, the intraperitoneal use of sulfathiazole somewhat lowers the morbidity after total abdominal hysterectomy, but it is much less important than vaginal preparation.

Appendectomy performed simultaneously with total abdominal hysterectomy has no effect on the morbidity and should be performed in all cases in which there is no contraindication.

ADNEXAL AND PERIUTERINE CONDITIONS

Clinical Notes on Benign Ovarian and Paraovarian Tumors Observed During the Period 1939-1949 (Note cliniche sui tumori ovarici e parovarici benigni osservati nel periodo 1939–1949). GIUSEPPE NICORA. *Minerva gin.*, Tor., 1950, 2: 319.

The author found 187 cases (3.45 per cent) of benign ovarian and paraovarian tumors among 4,825 gynecologic admissions to the Obstetric and Gynecologic Clinic of the University of Cagliari. The tumors included 5 papilliferous adenocystomas, 6 fibromas, 25 paraovarian cysts, 29 pseudomucinous adenocystomas, 30 retention cysts (27 follicular, 3 luteinic), 30 dermoid cysts, and 62 simple serous cystomas. Most of the tumors were unilateral; in 13 cases (6.52 per cent) both ovaries were involved, 10 times by the same type of tumor. This is in contrast with the 50 per cent bilaterality of malignant tumors.

In 18 cases (9.62 per cent) the tumor was associated with some phase of pregnancy. The youngest patient was 10 years of age. In 140 cases (74.84 per cent) the tumor occurred in patients 15 to 45 years of age, and in 42 cases (23.03 per cent), occurred in patients more than 45 years of age. Age played no specific role in the occurrence of the type of tumor. One hundred and twenty-four patients (66.30 per cent) had been pregnant, and it may be concluded that these tumors exerted barely any damaging influence on female fertility (15 cases, or 8.02 per cent), especially since causes of sterility in the husband were not regularly searched for, and some of the women had genital disorders which by themselves could explain the sterility.

In 47 patients (25.13 per cent) the increase in volume of the abdomen or the finding of a mass on palpation led to the discovery of the tumor, but not always in time to avoid complications, which occurred in 19 patients (40.35 per cent) and were due to torsion in 15 patients and to carcinomatous degeneration of a dermoid cyst in 1 patient, which had

been diagnosed 8 years previously. (In 3 patients the diagnosis was incorrect.)

In 81.62 per cent of the remaining 140 patients the tumor was revealed indirectly by pain, in 17.64 per cent by menstrual changes, and in the remainder by signs of compression, and intestinal and urinary disturbances. None of the 20 menopausal patients presented genital hemorrhages even in the presence of complications due to the tumor. The general condition of the patient on admission was good in 47 cases (25.13 per cent), fair in 41 cases (21.92 per cent), and poor in 99 cases (52.95 per cent). Ascites was found in 7 patients (3.74 per cent); its association with pleural effusion, having similar physicochemical characteristics (Meigs' syndrome), was observed in 1 case of fibroma.

Complications due to the tumor occurred in 103 patients (54.54 per cent) and included principally 60 torsions (32.08 per cent), 25 adhesions to neighboring organs (13.36 per cent), and 10 infraligamental developments (5.34 per cent). Torsion was acute in 75 per cent of the cases and rather chronic in 25 per cent. It occurred with about equal frequency in pregnant and nonpregnant women; in pregnant women it occurred during the first trimester in 72 per cent, and during the second trimester in 28 per cent. In the tumor itself, torsion caused parenchymal hemorrhage 14 times (23.34 per cent), necrosis 11 times (18.33 per cent), and inflammatory reactions leading to adhesions 8 times (13.33 per cent).

All tumors were treated surgically and the postoperative course was uneventful in 170 cases (90.90 per cent). There were 3 deaths (1.60 per cent).

RICHARD KEMEL, M.D.

Malignant Lesions of the Uterus Associated with Estrogen-Producing Ovarian Tumors. MALCOLM B. DOCKERTY and ELIZABETH MUSSEY. *Am. J. Obst.*, 1951, 61: 147.

The coexistence of uterine carcinoma and functioning, or feminizing, ovarian neoplasms has been observed by several writers and, in 1939, in a report on some of the first cases, the possible importance of estrogen as the carcinogenic agent was suggested. In a study of 87 granulosa cell and theca cell tumors, the authors noted the occurrence of uterine cancer 15 times; no less than 3 of the patients had had mammary carcinoma (bilateral on 1 occasion). The over-all incidence of the association of uterine and ovarian lesions was more than 15 per cent, and the figure reached 27 per cent when the patients who suffered the complication after the age of 50 years were considered. Uterine cancer did not complicate granulosa cell and theca cell tumors of younger women. This observation is important from the standpoint of treatment.

It appears that fundal carcinoma rarely occurs in experimental animals other than in rabbits of a certain group and this may account for the difficulty of inducing the lesions in other species by the administration of exogenous estrogens. On the clinical side it has been noted that uterine as well as mammary carcinomas are rarely observed after oophorectomy, even though the adrenal glands continue to supply estrogen in small amounts.

The association, in 3 instances, of a feminizing ovarian tumor with carcinoma of the breast, as well as of the endometrium, brought out still another feature of interest in the authors' study.

A series of 16 cases was presented in which functioning (feminizing) ovarian tumors were associated with the presence of uterine carcinoma. This association was much more frequent than that which could be explained on the basis of chance alone.

Carcinogenic influence of estrogen was suggested as a possible cause.

The prevalent literature on the subject was reviewed briefly.

EXTERNAL GENITALIA

Treatment of Vulvar Carcinoma (Zur Therapie des Vulva-Karzinoms). H. HUBER. *Geburtsh. & Frauenh.*, 1950, 10: 639.

At the Women's Clinic of Kiel University during the years from 1922 to 1947 there were 94 admissions for primary vulvar carcinoma; 79 of the patients were observed for 5 years. The radical operation with removal of the vulva and of the regional inguinal and femoral lymph nodes, usually unilaterally, was performed in 19 cases with a 5 year cure in 7 (36.8 per cent), 1 operative death, and 1 late recurrence. Conservative operations without removal of the inguinal lymph nodes were performed in 21 cases with a 5 year cure in 9 (42.9 per cent) and 2 late recurrences. Radium therapy was used in 18 cases with a 5 year cure in 4 (22.2 per cent) and 2 late recurrences. Roentgen therapy was given in 8 cases with a 5 year cure (12.5 per cent). No treatment was administered in 13 cases. Thus, among the 79 cases of primary vulvar carcinoma there were 21 five year cures (26.6 per cent), and among the 66 treated cases the 5 year cures amounted to 31.8 per cent.

The result of the treatment of vulvar carcinoma depends largely on the involvement of the regional lymph nodes. While beginning carcinoma has a relatively favorable prognosis, invasion of the efferent lymphatic system makes it rapidly unfavorable. This is evidenced by the statistics of other authors, and the present material shows only 1 case with 5 year cure after removal of carcinomatous inguinal nodes. The series shows that the curative results of operative treatment surpass those of any other method, and that the results of conservative operations are even better than those of radical operation, probably because in the patients so treated most of the tumors are circumscribed or early. Analysis of the cases submitted to radical operation shows that extension of the intervention to include the pelvic lymph nodes has not improved the results. Further study shows that the results of conservative operations and of radium application may be jeopardized by recurrence or late recurrence in precancerous lesions which should have been removed. In

these cases surgical removal of the tumor and endangered areas is indicated. In any case, treatment must be individualized, although radical operation remains the method that offers the best chances of success. It is still impossible to decide whether prophylactic roentgen irradiation has any unequivocal action on vulvar carcinoma. It should be noted that two fractures of the upper femur were possibly due to the effects of irradiation. RICHARD KEMEL, M.D.

MISCELLANEOUS

Sphincteric Function Established by Kinking of the Urethra. AXEL INGELMAN-SUNDBERG. *Acta chir. scand.*, 1951, 101: 1.

The author describes an operation he has developed for the treatment of urinary incontinence due to destruction or paralysis of the urethral sphincter. The method is one in which a kink in the urethra that is present only in the rest position of the bladder is substituted for the normal urethral sphincter action.

The operation consists of lengthening the urethra and placing the new part between the anterior surface of the symphysis and the bulbocavernosus muscle, in such a way that the urethra is kinked by the inferior edge of the symphysis. Of 10 patients on whom the operation was performed, 8 became completely continent, and the 2 other patients suffered only from stress incontinence.

ELY ELLIOTT LAZARUS, M.D.

The Lethal Dose of the Stilbene Substances in Experimental Animals (La dose letale degli stilbenici negli animali da esperimento). A. BORSÓ and P. MARZIALE. *Clin. ostet. gin.*, 1950, 52: 129.

Using rabbits weighing about 1 kilogram, the authors injected into the marginal vein of the ear a solution of a stilbene salt in a concentration of 20 mgm. of the substance per 5 c.c. vial (hydroestril forte) into the marginal vein of the ear of rabbits weighing about 1 kilogram. The contents of the vials were injected slowly, one after the other, and the phenomena which gradually occurred were observed. In the first 2 rabbits only two vials were used and during the injection intense myosis, fleeting tremors over the whole body, and numerous defecations were observed. For a few hours after the experiment the animals showed some sluggishness in their normal reactions, but they began to eat spontaneously again after about 5 hours and behaved normally on the following day.

The contents of four vials were administered to 3 other rabbits and during the injection of the first 10 c.c. the same phenomena were observed as in the first experiment. Then, as the injection continued the phenomena became intensified and at the end of the injection the animals could hardly stand on their legs, preferred to lie on their side, and did not respond to stimulation; their respiration always remained fast. About half an hour after the injection, the animals resumed their normal position, stood on their legs, but they remained immobile when stimulated. Let alone, they did not take food and died 6½, 8, and 10 hours, respectively, after institution of the treatment.

Fifteen days after the first experiment the 2 rabbits which had survived were given the contents of four vials; they showed the same symptoms as the animals in the second experiment and died in 7 and 12 hours, respectively.

Autopsy revealed small parenchymal hemorrhages, especially in the liver and kidneys of all 5 animals. Although the observations showed that the drug exercised a violent stimulation on the vagal system, the authors think that the cause of death lies rather in the parenchymal hemorrhages, because otherwise death should have occurred immediately after the injection. The changes in the vagal system seem to be compensable and reversible, as the animals in the two experiments presented the same symptomatology (varying in degree), which, however, stopped after about 4 hours in the first experiment and the animals recovered.

The certain lethal dose for the stilbene substances may be accepted as 80 mgm. massively injected into the circulation of rabbits weighing about 1 kilogram. The lethal dose for women must be correspondingly high and such as will never be reached in practice. However, attention is called to the dangers of protracted administration of the drug, especially when absorption cannot be voluntarily limited, as in the subcutaneous implantation of pellets.

RICHARD KEMEL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Observations on the Fetal Aspects of the Placental Circulation. SEYMOUR L. ROMNEY and DUNCAN E. REID. *Am. J. Obst.*, 1951, 61: 83.

Using a variety of injection techniques, the authors studied the vascular ramifications of the human placenta. Placentas injected with vinyl acetate have been corroded, and injections of india ink have been cleared.

The intimate nature of the relationships of the maternal and fetal vascular channels within the placenta was a major source of difficulty in the study of the uteroplacental circulation. The fetal capillary network, although extensive, is short in linear magnitude, and no large-sized veins could be identified. The capillary network of the subchorionic zone is sinusoidal in nature. The area adjacent to the decidual plate, in contrast, has a plexiform arrangement. This morphological discrepancy suggests diverse functional activity in the various zones of the placenta. ELY ELLIOTT LAZARUS, M.D.

The Epithelia of the Pregnant Cervix. LEON A. CARROW and R. R. GREENE. *Am. J. Obst.*, 1951, 61: 237.

The stratified squamous and endocervical epithelia from the cervices of 96 pregnant women were studied. Sixty-four of these patients had normal-appearing cervices; 32 had some gross lesion on the cervix.

Although hyperplastic alterations of the epithelium of the endocervical canal and glands were noted, these changes could not be considered specific for pregnancy since they were frequently seen in nonpregnant specimens also.

Epidermization was noted in slightly over half the cases studied. Atypical forms of epidermization were compared and contrasted with the microscopic picture of carcinoma.

No typical pregnancy changes were noted in the stratified squamous epithelium. The incidence of hyperactivity as manifested by increased general thickness, increase in basal-cell layer, and frequency of mitoses is discussed.

It is concluded that when the criteria for the diagnosis of carcinoma of the cervix are present, this diagnosis is valid irrespective of whether the patient is or is not pregnant. JOHN R. WOLFF, M.D.

The Role of Marginal Sinus Rupture in Antenatal Hemorrhage. JOHN S. FISH, R. A. BARTHOLOMEW, E. D. COLVIN, and WILLIAM H. GRIMES. *Am. J. Obst.*, 1951, 61: 20.

Rupture of the marginal sinus of the normally implanted placenta was found to be responsible for one-third of all cases of antenatal hemorrhage occurring in the last trimester or in labor. Rupture of the marginal sinus, accounting for many of the antenatal hemorrhages heretofore classified as of unknown origin, closely simulated placenta previa. The fragile membranous structure of the marginal sinus renders it susceptible to rupture under conditions of stress which would not ordinarily result in placental separation. It is probable that rupture of the sinus, rather than placental separation, is the actual cause of the bleeding in many cases of placenta previa, and can be demonstrated to be the usual cause in cases in which the placenta is normally implanted. The frequency of antenatal hemorrhage due to ruptured sinus progressively increased in each successive month of the third trimester, but was highest during labor.

Placenta previa showed a higher incidence of bleeding before labor and ruptured marginal sinus a higher incidence of bleeding during labor. Rupture of the marginal sinus showed a greater tendency to bring on labor than placenta previa, both at and before term. Hemorrhage due to ruptured sinus showed less tendency to recurrence than placenta previa, but it simulated placenta previa in respect to absence of pain and the bright and profuse character of the bleeding. Gross hemorrhage was more frequent in ruptured sinus than in placenta previa. Evidence of associated toxemia was present in 64.3 per cent of the cases of abruptio placentae, but was of no more than average incidence in placenta previa and rupture of the marginal sinus.

Of the three most important causes of antenatal hemorrhage of late pregnancy—rupture of the marginal sinus, placenta previa, and abruptio placenta—rupture of the marginal sinus was attended by the lowest fetal mortality (4 per cent). There was no maternal mortality. Expectant management, of proved value to mother and fetus in placenta previa, is even more applicable to the hemorrhage of ruptured marginal sinus, in which the risk to the mother and baby is much less, provided that the blood losses are replaced. It is not applicable to the hemorrhage of abruptio placenta since this condition is not of a toxic nature, but usually terminates or requires the termination of pregnancy at once. CHARLES BARON, M.D.

The Morphological Changes in the Cervix During Pregnancy, Including Intraepithelial Carcinoma. JOHN W. W. EPPERSON, LOUIS M. HELLMAN, GERALD A. GALVIN, and TRENT BUSBY. *Am. J. Obst.*, 1951, 61: 50.

The morphological changes in the pregnant cervix have never been completely studied, and have never been followed throughout pregnancy and the puerperium. In order to make a systematic study of both the glandular and stratified squamous epithelial changes during the prenatal period, at delivery, and in the puerperium, the authors took punch

biopsies at various intervals during these periods. It had been feared that biopsies would cause profuse hemorrhage, abortions, or infections, but this study proved these fears to be unfounded.

The gestational changes in the human cervical stroma consist of edema, increased vascularity, a high frequency of leucocytic infiltration, and a 10 to 20 per cent incidence of decidual reaction. In the glands, pregnancy causes hyperplasia of the epithelium, hyperplasia of the glands, and adenomatous hyperplasia. In addition, epidermization occurs in about 14 per cent of the cases. There is an increased vascularity and edema of the epithelium. Basal cell hyperactivity occurs in 19 per cent of all pregnant individuals. Whether this is an increased incidence of this condition over the incidence in the nonpregnant woman the authors could not state.

There were at least 5 instances of a type of alteration which in nonpregnant women would be called "intraepithelial carcinoma." These occurred during a 2 year period in which 4,849 deliveries occurred. This gives an incidence of 0.1 per cent which is double the usually cited instance. Of great interest is the fact that, although these patients were allowed to go through their pregnancy, all appeared normal at postpartum biopsy.

ELY ELLIOTT LAZARUS, M.D.

LABOR AND ITS COMPLICATIONS

Unanticipated Fetal Risks in the Perineal Stage of Labor. JAMES A. HARRAR and MYRON I. BUCHMAN. *Am. J. Obst.*, 1951, 61: 348.

The obstetrician has every reason to expect a normal infant once the vertex has reached the perineum after a normal labor and an uncomplicated antepartum course. In a study of 52,120 deliveries the authors found a 5 per cent unanticipated fetal death rate.

Cord complications rank highest as a cause of death at this stage. Other causes in their order of frequency are late premature separation of the placenta, shoulder dystocia, and a prolonged second stage with excessive sedation.

Fetal death was always signaled by bradycardia and the presence of fresh meconium. These signs herald profound and terminal anoxia, and must be carefully watched for and properly dealt with.

ELY ELLIOTT LAZARUS, M.D.

Fetal Mortality in Cesarean Section (La mortalidad fetal en la cesárea). VALENTIN ALONSO ROMEO and CASIMIRA SEGURA DE ALONSO. *Rev. espan. obst.*, Valencia, 1950, 9: 323.

This paper represents a study of the factors involved in the death of infants delivered by cesarean section. It is based on 167 sections performed from 1940 to 1949 at the Casa Provincial de Maternidad de Barcelona. The authors have considered not only the various factors of maternal health during gestation and the conduct of labor, including anesthesia, but have taken into account autopsies on the dead infants.

The causes of death of the 13 fetuses (a fetal mortality rate of 7.78%) were given as follows: craniocerebral lesions in 4, pneumonia in 2, sepsis in 1, anemia in 1, hydrocephalus in 1, prematurity in 1, maternal diabetes in 1, cause undetermined in 2 fetuses.

The conclusions arrived at from the study indicate that trial labor should not be permitted in pelvic dystocia when the disproportion is severe, and should not be permitted longer than 6 hours after rupture of the membranes in less obvious disproportions. Signs of fetal embarrassment should lead to prompt delivery.

Local or regional anesthesia was recommended, and is preferred by these authors. If general anesthesia is employed, it should be as light as possible, and carry ample oxygen. Curare is useful as a supplement to such agents.

A pale infant should suggest transplacental hemorrhage, particularly in the presence of a placenta previa or premature separation of the placenta. Blood transfusion in adequate amounts is required for such infants. All maternal diseases should receive careful control. In erythroblastosis (except fetal hydrops), total blood replacement is recommended.

The details upon which these conclusions are based are given in table form, and their interpretation is sufficiently elaborated upon to lead to the conclusions outlined. HIRAM T. LANGSTON, M.D.

NEWBORN

Perinatal Mortality in Toxemia of Pregnancy (Perinatální úmrtnost při toxikosách matky). LUDVÍK HAVLÁVEK and ALOIS VAŠIČKA. *Cesk. gyn.*, 1950, 10: 677.

The material here considered consists of data gathered by questionnaire from the obstetrical institutions of Bohemia, Slovakia, and Moravia. In more than 100,000 deliveries, there were observed more than 1,000 cases of toxemia of pregnancy in the past 3 years. Much of this material, however, was not usable for the purposes of this study, because of insufficient data and a lack of standards for diagnosis and classification.

The figures here reported did, however, indicate, for certain forms of the syndrome of toxic pyelitis, a difference in hygienic and other health conditions for the different regions, and a difference in the neurovegetative constitution (emesis and hyperemesis gravidarum) in the mothers themselves. In this regard, the greatest lability is noted for the women of Moravia. Thus, for Moravia and for the few regions of Bohemia and Slovakia showing such excess of neurovegetative lability, the authors recommend a greater use of hospitalization.

The incidence of toxemia was highest in women between 20 and 30 years of age, and in those engaged in heavy physical labor (agricultural workers); for these, better antenatal care is recommended. About

a third of all patients had had no medical supervision (diet) at all during the period of pregnancy. Particularly important in the matter of medical supervision during the pregnancy are those patients who give a history of previous disease which might affect the heart or kidney of the pregnant woman. Nearly a quarter of the women suffering from nephropathy had some renal damage following scarlet fever, diphtheria, thyrotoxicosis, and various infectious diseases. Especially prone to toxemia are the pyknic types, multipara, those who have had previous abortions, or premature or complicated deliveries.

Perinatal mortality, that is, prenatal, neonatal, and postnatal child mortality, for all forms of toxemia and for all the regions included in the figures, is estimated at about 9.2 per cent. Six pregnancies were interrupted artificially—3 times for hyperemesis, once for nephropathy, once for psychosis of pregnancy, and once for chorea. Altogether, 145 of the 183 infants that died (where sufficiency of data permitted inclusion in this study) were alive at birth; 85 died at birth and 60 died in the postpartum period. Of the 21 infants living at birth, who were delivered by abdominal cesarean section, 3 died during delivery and 18 died postpartum. All 5 infants delivered by vaginal cesarean section died (2 during delivery and 3 after). Of the 13 infants delivered by version and extraction, 1 was dead before delivery, 9 died during the operation, and 3 later. Of the 6 infants delivered by forceps, all died (4 during the operation and 2 later). Thus it seems that cesarean abdominal delivery is the least, and forceps delivery the most, dangerous procedure.

Autopsy examinations were made on 106 of the dead infants. On the whole, the postmortem findings were not characteristic. Most frequently encountered was hemorrhage into the meninges (49 infants), the brain (47 infants), and into other organs (29 infants). Death of 36 infants was found to be due to intrauterine asphyxia, 24 infants were macerated, and in 46, the cause of death was diagnosed as debilitas vitae. It is with this last diagnosis that the authors are dissatisfied, and they suggest a painstaking postmortem study of all infants dying perinatally, especially those who have been operated upon, both to justify the indications and to seek the cause of death. JOHN W. BRENNAN, M.D.

Perinatal Mortality in Breech Presentations Delivered by the Classical Method (Perinatální úmrtnost u porodů koncem pánevním vedeným methodou klasickou). ERNA PETROVSKÁ. *Cesk. Gyn.*, 1950, 11: 770.

Breech presentation (421 cases) comprised 3.8 per cent of 10,934 births at the author's institution. Some 765 cases of breech presentation were collected from other sources, but in this material difficulties were encountered in adapting the figures to those of the author's material, and they are not included in the computations. In this outside material, however, the results were not so divergent as to demand a lengthy separate discussion.

Of the 421 breech deliveries, 383 were by the classical method of Mauriceau-Smellie and 38 were by extraction. The extraction in each instance was indicated by serious conditions of the mother or child. Of these 38 serious cases, 33 had manual extractions by the method of Martin-Wiegand, or Martin-Wiegand-Winckel, and 5 deliveries were performed with the Kjelland forceps.

The total perinatal mortality for all cases (421) was 15.6 per cent; here, however, after exclusion of the macerated fetuses, of those with erythroblastosis, malformations, nonviability, and prematurity (the so-called irreducible minimum of Potter), the reduced total mortality was found to be 3.3 per cent. The total mortality for the 383 Mauriceau-Smellie deliveries was 12 per cent (reduced: 3.68 per cent); for the 38 extractions the total mortality was 52.6 per cent (reduced: 31.6 per cent). Of the 5 infants delivered by forceps, 1 died.

The most important cause of infant mortality in the author's material was intracranial injury (hemorrhage, lacerations, etc.); the next most important cause was asphyxia.

It is considered that the method of Mauriceau-Smellie is ideal for properly selected cases. The method of Bracht is proper for small fetuses, but for the large child the Mauriceau-Smellie maneuver is necessary; it forestalls deflection of the head, presents optimal relationships with reference to the diameters of the head and of the pelvis, and thus spares the head of the child from unnecessary stresses. These considerations, of course, apply also to the matter of the soft tissues of the birth canal. In the Bracht procedure, the suprapubic pressure on the child's head, which is an indispensable integer of the method of Bracht, can hardly be designated physiological; therefore, this operation is not proposed unless it is unavoidable.

Breech deliveries still present a high mortality rate for the infant and require further study and a better control of pregnancy. The suggestion of the Spanish-American authors for a pharmacologic approach—the so-called "version" in the course of the pregnancy by means of purgatives—is interesting; however, it is of no practical value as the results are not dependable. Much more important is roentgenology and pelvimetry and an exact control of the pregnancy, especially during the ultimate weeks, which may save the life of the child even in unfavorable cases. JOHN W. BRENNAN, M.D.

Infant Mortality in Breech Presentation Delivered by Bracht's Method (Dětská úmrtnost u porodů koncem pánevním, vedených podle Brachta). EMANUELA GRÉGROVÁ. *Cesk. gyn.*, 1950, 11: 792.

In an attempt at comparing the results to be expected from the method of Bracht (*Zbl. Gyn.*, 1936, 5: 302) in breech presentations with those of the classical method, an extensive material was procured from the hospitals and obstetrical departments of universities—one for those using the Bracht method and one for those using the classical method.

After the usual reductions for attaining as near as possible the irreducible minimum of Potter, it was found that the perinatal mortality for the Bracht method was 3.60 per cent, as compared with 6.15 to 6.17 per cent for the classical method.

These figures indicate an essential reduction in infant mortality with use of the Bracht method, in addition to the obvious reduction in infant morbidity and even in maternal infections. The objection to the Bracht method—of the increased incidence of intracranial injury—seems answered by the autopsy figures from the author's own material at the Third Obstetrical Clinic of Charles University, Prague, Bohemia, where the cause of death was found to be cerebral hemorrhage in only 9 per cent of cases. This suprapubic pressure on the after-coming head in the Bracht method is the only objection to an otherwise physiological procedure.

The author concludes that the Bracht method of delivery for patients with breech presentation should be applied to all uncomplicated cases.

JOHN W. BRENNAN, M.D.

MISCELLANEOUS

The Question of Superfetation and Abortive Ova in Multiple Pregnancies; Report of a Case and Review of the Literature (Zur Frage der Superfetation und der Abortiveier bei Mehrlingsschwangerschaften; Bericht ueber einen Fall and Literaturuebersicht). K. SALFELDER and H. J. LAMBERTZ. *Geburtsh. & Frauenh.*, 1951, 11: 50.

The authors report the case of a woman 37 years of age who had an abortion in the fourth month of pregnancy. Two fetuses were expelled, one 14 cm. in length, the other 0.9 cm. in length. The histologic examination of the placentas showed that both placentas were in the same stage of development, which fact proves that this was not a case of superfetation, but of twins, in which one of the twins was retarded in his development. A further fact which disproves the assumption of superfetation in this case was that the smaller of the embryos was far too large for an assumed age of 4 to 5 weeks.

Cases of superfetation (second conception during pregnancy by fecundation of an ovum of a later ovulation period) have been repeatedly reported. The authors review 27 cases from the literature and have shown that in none of these could superfetation be proved beyond doubt. They believe that all these cases were in reality multiple pregnancies in which one embryo failed to develop at a normal rate for one cause or another. Defects of the germinal plasma or lethal factors may be responsible for the retarded development of one of the embryos. Furthermore, a constitutionally normal ovum may be damaged by disturbances in circulation of the placenta. In this connection it is noteworthy that hemorrhages during pregnancy have been reported frequently in alleged cases of superfetation.

Although the occurrence of superfetation has been proved in experiments on rabbits, the authors believe that no case has been confirmed in man. They state that, for various reasons, it will always be extremely difficult to prove that an individual case of 2 embryos or newborn infants in different stages of development is caused by superfetation rather than by multiple pregnancy. According to these authors, the fact of superfetation could be considered as proved beyond doubt only if two fathers of different races were involved, and if the embryos or newborns would show their respective racial traits.

WERNER M. SOLMITZ, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Progress in the Diagnosis of Kidney Function (Fifth Report): The Effectiveness of Determination of the Buffer Capacity in the Pyelic Urine for Early Diagnosis of Surgical Kidney Diseases (Fortschritte in der funktionellen Nierendiagnostik (V. Mitteilung): Die Leistungsfaehigkeit der Pufferkapazitaetsbestimmung im Nierenbeckenurin zur Fruehdiagnose chirurgisch kranker Nieren). SIEGFRIED RAABE. *Zschr. Urol.*, 1951, 44: 30.

In a previous report the author described a colorimetric micromethod permitting the exact titration of the smallest amounts (one drop) of urine from the kidney pelvis. This method makes it possible to analyze exactly the amount of excretion of different alkaline and acid salts.

In the present article the technique and normal curve of "phosphate titration" are described and the value of the titration for early diagnosis of surgical disturbances of the kidney is shown in 8 cases which are reported in detail. Twenty cubic centimeters of an 18.5 per cent monosodium phosphate solution are injected intravenously, the urine from both sides is collected separately, and the buffer capacity is measured in 3 minute intervals for 15 minutes and recorded in a graph. Three different values can be determined by the phosphate method: (1) titrated alkaline substance (S_1), (2) titrated acid substance (L_3), and (3) entire titrated substance (K_t). Of these three, the amount of acid substance (L_3) is best suited for evaluation of the kidney function. The higher the concentration of excreted acid substances rises in the pyelic urine, the better is the function of the kidney. This method is superior to all other function tests including the mere determination of the *p*H in the pyelic urine (Rehn test). It could be shown that in some cases in which the Rehn test did not show any difference between the sides, the phosphate method indicated clearly which kidney was the diseased one.

Eight cases are discussed in which intravenous and retrograde pyelography, the indigocarmine test, and titration of the *p*H of the pyelic urine failed to show a difference between the two sides, and only phosphate titration clinched the diagnosis. They included: paranephritic abscess, pyonephrosis, kidney stone, kidney carcinoma, hypernephroma, kidney tuberculosis (2 cases), and hydroureter caused by obstructing adhesions after purulent appendicitis.

In summarizing, the author states that unilateral disturbances can be diagnosed by phosphate titration in the early beginning when all other methods fail. On the other hand, the method will show that the function of a kidney is entirely normal in cases in which other methods leave a doubt or give misleading results. This is true especially for the methylene blue method which was correct only in 70 per cent of the cases in which it has been used.

A further advantage of the phosphate method is that it permits, by frequently repeated tests, evaluation of the course of a pathologic process. If the difference between the titration curves of both sides increases, or, in other words, if the original low L_3 curve of the diseased side goes down further in a later examination, proof for a progressing process is given and operation is indicated. If the difference between the sides remains constant, it can be assumed that the pathologic process is arrested and is in the process of healing. If an originally low L_3 rises gradually complete recovery can be assumed.

This very interesting article should be studied in the original. WERNER M. SOLMITZ, M.D.

Renal and Ureteral Calculi: a Study of the Occurrence in Sweden from 1911 to 1938, with Some Notes on the Geographical Distribution. INGE HEDENBERG. *Acta chir. scand.*, 1951, 101: 17.

The author presents a very complete statistical study of the occurrence of primary (noninfectious) renal and ureteral calculi in Sweden during the period from 1911 to 1938. During this period the frequency of renal and ureteral calculi expressed as per 100,000 inhabitants has increased 11.6 times. However, this increase can be explained by the increased hospital admissions, improved diagnostic means, improved communications, and altered indications for hospitalization of patients suspected of having renal and ureteral calculi, and is not a true increase in the frequency of the disease. The report is based on the study of 43,547 cases of renal and ureteral calculi admitted to Swedish hospitals.

JOSEPH E. MAURER, M.D.

The Diagnostic Value of Aortography in Renal Tumors (Considerações a propósito do valor diagnóstico da aortografia nos tumores renais). ANTÓNIA CARNEIRO DE MOURA. *Gaz. méd. Port.*, 1950, 3: 913.

Two cases of tumors of the right kidney are reported—in 1 case, a myxoblastic sarcoma in a 34 year old woman, and in the other, a huge Grawitz tumor in a 65 year old man. These patients were examined preoperatively by means of aortography. The technique of this method is discussed in detail in the English language by Nelson (*Surg. Gyn. Obst.*, 1942, 74: 655), who discusses the manifestation of pooling, or laking, of the opacified blood in the blood sinuses of the renal tumor—especially of the Grawitz tumor—which is of value in the differentiation of these tumors from tumors of other nature (papillary tumors of the renal pelvis; renal tumors without such blood sinuses).

In the case of the sarcoma, the method showed the poverty of sanguineous irrigation of the neoplasm, a distinction which could not be definitively made with ascending pyelography. In fact, in neither of these tumors does ascending pyelography

satisfactorily clarify the diagnosis; the sarcoma was at first suspected of being a pararenal new growth.

The aortography in these instances afforded a much more detailed and subtle elucidation of the conditions encountered at operation. In the Grawitz tumor the exact position of the blood vascular pedicle could be determined, permitting of a more facile and advantageous transperitoneal ligation of the blood supply of the kidneys; in this manner the attack upon, and removal of, the mass transperitoneally enabled a much cleaner and safer extirpation than could be expected by the attack from the flank.

The author considers that the method, with use of an 80 per cent solution of sodium iodide, is entirely innocuous and full of promise. In fact, he believes that with sufficient experience the method may enable the making of a preoperative diagnosis of the histologic nature of the neoplasm.

JOHN W. BRENNAN, M.D.

A Contribution to the Technique of Pyeloureteral Neoanastomosis and Ureteroureteral Anastomosis. MORTEN H. GJESSING. *Acta chir. scand.*, 1951, 101: 37.

The author presents a new technique of anastomosis between the ureter and renal pelvis in cases of hydronephrosis due to ureteropelvic obstruction. The ureter is severed from the pelvis and the end is split; the pelvis is then resected, if excessively redundant, and an oval opening is made at the most dependent portion. The ureteral flaps are drawn through this opening, are brought again outside of the pelvis through two small slits, and are sutured there. The advantages of this procedure are said to be simplicity, a large anchoring area, nonpenetrating sutures, and the ability to provide a suitable take-off angle from the pelvis. Two cases are reported.

JOSEPH E. MAURER, M.D.

Artificial Kidney: Preliminary Report. OSWALD S. LOWSLEY and THOMAS J. KIRWIN. *J. Urol.*, Balt., 1951, 65: 163.

The history of the development of the various types of artificial kidneys is reviewed in most instructive detail. The authors have attempted to eliminate the physical and mechanical difficulties that were noted in previous machines. They have constructed a reasonably compact and apparently very efficient artificial kidney which can be moved easily, permits simple sterilization, and holds 38 gallons of electrolyte solution that may be used over and over again during the period of dialysis.

Nitrogenous products were removed promptly during in vitro experiments and trials on both animals and human beings. It was possible not only to remove electrolytes, such as sodium and potassium, but to increase their content in the blood by raising their concentration in the dialyzing solution.

Only 300 c.c. of the patient's heparinized blood is contained in the dialyzer at any time. This is removed from the anticubital veins through polythene cannulas and is moved through the machine at an easily controlled rate of flow by a mechanical pump. The apparatus also contains thermostatic equipment that automatically controls the temperature of the electrolyte solution.

After routine preliminary heparin tolerance tests, this artificial kidney was used in a variety of clinical cases, including some conditions associated with mild cardiac decompensation. Calcium gluconate was given intravenously when the electrolyte solution contained no calcium. No unfavorable reactions of any kind were noted during any of the clinical trials with this machine.

ORMOND S. CULP, M.D.

Retrocaval Ureter: Report of 4 Cases and Review of the Literature. JOHN E. HESLIN and CHRISTOPHER MAMONAS. *J. Urol.*, Balt., 1951, 65: 212.

This congenital anomaly of the venous system in which the ureter passes behind the inferior vena cava has been reported in 40 cases, all of which, except 1, occurred on the right side. Hydronephrosis resulted in three-fourths of these cases.

The kidney in its ascent from the pelvis to its normal position passes through a ring of veins. If either the ventral limb of this ring persists or if the dorsal limb fails to develop, a retrocaval ureter will result.

The symptoms, when present, are those of obstruction and hydronephrosis with pain in the flanks, frequency, nocturia, hematuria, and pyuria. This possibility must be considered in a hydronephrosis on the right side. Roentgenogram is almost pathognomonic. Anterior ureteropyelography reveals hydronephrosis with a long proximal segment of the ureter and medial dislocation of the ureter to or beyond the midline, beginning with the third, fourth, or fifth lumbar vertebra. A distinct hook or S-curve is imparted to the ureter. In lateral views the ureter becomes anterior to the vertebral bodies at the third lumbar vertebra.

Surgical therapy is indicated only if a hydronephrosis is present, and consists of nephrectomy in the advanced cases or attempts at renal conservation in the cases with a partially damaged kidney or inadequate renal reserve. These attempts at conservation may be classified as (1) division of the hydronephrotic segment above the ureteropelvic outlet, with replacement of the distal segment and anastomosis anterior to the vena cava, (2) division of the ureter at the ureteropelvic junction and anastomosis in its normal position, (3) division below the ureteropelvic junction, (4) division of the ureter with excision of the diseased segment behind the vena cava and anastomosis anterior to the vein, or (5) division of the ureter at the vesical junction, unwinding it from behind the vena cava and reimplanting it into the bladder. Because the first procedure reduces the possibility of postoperative stricture, it is the procedure of choice. Difficulties encountered during repair are: interference with the blood supply of the ureter when it is stripped from

behind the vena cava, danger to the vein itself, and stricture at the area formerly behind the vena cava and at the level of the anastomosis. The hazards of Harrill's operation (the procedure of choice), such as ureteral stricture, stone, and infection, are somewhat alleviated by antibiotics, ureteral splinting, and pyelostomy drainage.

This entity should be treated as any other congenital anomaly. Only when pathological changes result should surgery be considered.

The authors report 4 additional cases, in 3 of which the treatment was successful; 1 patient refused treatment. HERBERT J. KAROL, M.D.

A Rare Case of Primary Fibrous Tumor of the Ureter Protruding into the Bladder (Raro caso di tumore connettivale primitivo dell'uretere procidente nella vescica). PAOLO CAVAZZANA. *Arch. ital. urol.*, 1950, 24: 313.

A 21 year old unmarried woman suffered an attack of hematuria which ceased spontaneously after 5 days. Ten months later the bleeding returned with greater intensity. This hemorrhage lasted, with brief intervals of cessation, 15 days. The roentgenologic examination without opacification disclosed nothing. The descending pyelogram with uroselectan-B given intravenously disclosed irregular dilatation of the right ureter in its lower portion, the dilated portion measuring from 8 to 10 cm. In this segment could be made out a roentgen transparent material which seemed to protrude by its expanded end into the bladder. As a matter of fact, this mass intruding into the bladder could be examined directly by cystoscopy. It had a length of 2 cm. and a maximum diameter of 7 mm. The formation was covered with a normal-appearing mucosa of the ureter except at the apex where it had apparently ulcerated and was now a mass of granulations. The mass would show a sort of wavy motion every 10 to 15 seconds (ureteral peristalsis), but did not increase in size.

At operation the ureter was found to be enlarged as far as the bifurcation of the common iliac artery, and within it could be palpated through the uninfiltrated ureteral walls the contained tumor which was of uniform, elastic consistency and tended to slip away under the pressure of the finger. Everything suggested a benign new growth and the operation was conducted on conservative lines. The ureter was opened for about 2 cm. and the mass extracted *in toto* through this opening. The tumor was implanted in the ureteral mucosa by a small base, but nowhere was there evidence of tumor cell infiltration. The pull at the point of insertion had prolapsed the mucosal wall above it downward for a distance of about 2 cm.; this was excised together with the tumor mass itself, and terminoterminal reunion of the ureter was accomplished with interrupted sutures.

Twenty-three days after the operation, chromocystoscopy and descending pyelography showed a moderate degree of atony of the lower end of the right ureter, which was, otherwise, perfectly permeable and was functioning well.

The tumor upon histologic examination was found to be composed of a rather lax edematous, areolar tissue permeated with a few fibroblasts. The new formation was covered with a single layer of low epithelium which exhibited irregularly interrupted areas. The axial portion of the mass was formed of a more compact connective tissue carrying fine longitudinal blood vessels from the area of the mucosal prolapse to the termination of the tumor itself. At this latter point these blood vessels became highly interlaced and dilated; however, the author believes that this formation was the result of the congestive effects from the pressure of the sphincter of the vesicoureteral orifice, rather than any tendency toward an angiomatous transformation.

JOHN W. BRENNAN, M.D.

BLADDER, URETHRA, AND PENIS

Marion's Disease, or Bladder Neck Stenosis. E. MUSARD NANSON. *Austral. N. Zealand J. Surg.*, 1951, 20: 215.

Marion's disease, or obstruction of the neck of the bladder without prostatic enlargement, has been previously described as median bar, stenosis of the bladder neck, fibrous neck contractures, or fibrous prostate.

The two recognizable types of this disease are the congenital and the acquired. A diaphragm is present across the internal urethral meatus in the congenital form and consists of fibrous and muscular tissue without prostatic glands. There is no evidence of previous inflammatory reaction. The acquired form reveals scarring and fibrosis of the bladder neck with some prostatic glands and frequent evidence of previous inflammation.

The author reports a series of 84 cases seen between 1935 and 1948 with an average age incidence of 55 years. Although the congenital cases may be seen at an early age, approximately 20 years frequently elapse before consultation is sought. These patients present a history of a poor stream since childhood. Females are not infrequently seen with bladder neck stenosis.

Symptoms of this condition may be divided into three groups: (1) disorders of micturition due to failure of the bladder neck to open, as evidenced by a poor stream, dysuria, and straining, (2) disorders due to incomplete emptying of the bladder and back pressure as evidenced by chronic retention, nocturia, and frequency, and (3) disorders due to infection in stagnant urine which are evidenced by recurring attacks of acute cystitis. Back pressure with dilatation of the upper urinary tract and resulting renal failure is evidenced by anorexia, thirst, nausea, and constipation, and is uncommon except in children. This is because a diverticulum, which is more easily formed in later life, acts as a buffer and compensates for the increased bladder pressure without the necessary back pressure referred to the upper tract. The

gonoccocus is the most frequent organism causing the acquired type of stenosis.

Provided that neurological lesions can be excluded, the diagnosis is based on a normal prostate of normal consistency, the presence of residual urine, trabeculation, and diverticula. The presence of a diverticulum spells bladder neck stenosis until proved otherwise. A diverticulum is frequently the true cause of recurring cystitis and is the reason why at cystoscopy the bladder cannot be washed clear. A cystogram with radiopaque material will reveal the presence of the diverticulum, its size and site, and also the amount of residue remaining after spontaneous voiding of the dye.

Preparatory to surgical correction, bacteriological examination of the urine, determination of the blood urea nitrogen, and intravenous pyelograms are of importance. The most frequent infecting organism in this series was the Bacillus coli, followed by the Staphylococci albus and aureus. Should the urea nitrogen be elevated, preliminary catheter drainage of the bladder will be necessary.

In the absence of diverticula, transurethral resection of the bladder neck is the treatment of choice. Transvesical excision of the bladder neck, wedge resection, or simple prostatotomy with a deep posterior midline incision of the bladder neck are frequently satisfactory. If diverticula are present and if they are large, chronically infected, or do not empty properly, they should be excised by either the transvesical or extravesical approach. The diverticulectomy can either be done concurrently with the relief of the bladder neck obstruction, or primarily, with the relief of the obstruction at the second stage and bladder drainage in the interim.

HERBERT J. KAROL, M.D.

The Genesis of Vesicourinary Reflux (A proposito della genesi del reflusso vescico-ureterale). SAVA PETKOVIC. *Urologia*, Treviso, 1950, 17: 535.

The author considers the role of urinary reflux as a physiologicopathological phenomenon and its role in ascending infection.

Vesicoureteral reflux is thought to be exceedingly unusual in the normal individual and to exist only on the basis of a ureterovesical dyskinesia, perhaps on the basis of inflammation. The author was unable to find it in any normal subjects. Reflux will not occur in cadaver bladders even when pressure is raised to rupture them. Active bladder contractions are necessary for reflux which will not occur in the atonic bladder. Reflux is more likely to occur with small bladder volumes.

The oblique intramural course of the ureter is believed to play a major part in preventing reflux because in rabbits and cats, which have a short intramural ureter, reflux is common, while man, with a long intramural segment, shows such a phenomenon only rarely. The barrier to reflux in the normal individual consists of 3 main factors: (1) the actively contracting bladder musculature which compresses the intramural ureter, (2) the intravesical pressure which does the same, and (3) a functional muscular synergism between the bladder and ureter.

Lesions at the ureteral orifice may result in reflux. Marion has classified these into 4 groups: (1) congenital, (2) traumatic, (3) inflammatory, and (4) long-standing pressure such as prostatic obstruction.

The author then discusses these four groups in detail, presenting clinical and experimental situations. He stresses the frequency of reflux in congenital anomalies of the genitourinary tract, pointing out that the mesodermal origin of the trigone and the endodermal origin of the bladder may account for many cases of anomalous reflux.

GEORGE NARDI, M.D.

Congenital Exstrophy of the Urinary Bladder; Late Results of Treatment by the Coffey-Mayo Method of Ureterointestinal Anastomosis. B. MARVIN HARVARD and GERSHOM J. THOMPSON. *J. Urol.*, Balt., 1951, 65: 223.

"Statistically, 50 per cent of all persons afflicted with congenital exstrophy of the bladder are dead by their tenth year, and 66.6 per cent of them are dead by their twentieth year." These figures, quoted by C. H. Mayo in opening a discussion in 1925, have long been accepted in the prognosis for individuals born with an exstrophic urinary bladder.

In 1947 a patient who had undergone bilateral ureterosigmoidostomy and cystectomy for congenital exstrophy at the Mayo Clinic 35 years previously, came under the observation of the authors. This patient had been the first to undergo such treatment at the Clinic, and the second one of record to sustain ureteral transplantation along technical principles laid down by Coffey, the operation on the first having been performed by Middleton on March 1, 1911.

In the vast literature on this subject there is a conspicuous lack of studies relative to the long-term status of patients with an exstrophic urinary bladder and subsequently treated by ureterointestinal diversion of the urinary stream. As this patient eventually came to nephrectomy, it was decided that investigation might reveal others whose subsequent course had necessitated surgical intervention. Too, such a study might reveal valuable information relating to morbidity arising as a direct result of ureteral transplantation, longevity, and general state of being of this group of patients. Accordingly, a questionnaire was sent to all patients who had undergone bilateral ureterosigmoidostomy at the Mayo Clinic from 1912 through 1946.

Congenital exstrophy of the urinary bladder has been defined as a malformation found in both sexes, in which the anterior wall of the bladder and that portion of the anterior abdominal wall over it are missing, so that the inner surface of the posterior wall of the bladder protrudes on the abdomen and the ureters expel urine externally. All patients in this series had deformities commensurate with this definition, and no attempt was made to classify them further. The cause of exstrophy is unknown. Many theories have been advanced to explain its presence.

Their very number readily attests the lack of fundamental knowledge in this respect. It is a rare condition, being said to occur approximately once in every 40,000 births. Males, it is generally believed, are afflicted five times more frequently than females.

The final answer to the problem of surgical treatment of congenital exstrophy of the bladder has yet to be written. The writing of scores of surgeons and the wide variety of technique employed during the past century readily attest to this fact. The authors' study does not attempt to give the answer, but merely reviews the late results obtained with the Coffey-Mayo technique as one of the many surgical approaches to the problem.

One hundred and ninety-eight patients in more than 1,500,000 admissions to the Mayo Clinic were found to have exstrophy of the bladder. One hundred and forty-four of these were treated by ureterointestinal anastomosis. Males predominated over females 2 to 1. The ages of those undergoing operation varied from 10 months to 49 years, with most patients undergoing operation in the first and third decades. The postoperative mortality rate was 10.5 per cent for the 133 patients who underwent the two-stage operation. Well over 60 per cent of the total number of postoperative deaths (18 deaths) were of renal origin. Sixty-five per cent of the deaths that occurred after the patient left the hospital were ascribed to renal failure. A little more than two-thirds of 69 patients who survived operation and were living on January 1, 1947 gave more or less evidence of having pyelonephritis. In 41 postoperative excretory urograms dilatation of the kidneys and ureters was about equally common on the two sides. Nonvisualization was more common on the left side, while stones were encountered more often on the right. Four of 198 patients had carcinoma of the exstrophic bladder. Eighty-five of 98 traced patients on whom operations had been performed had survived for 5 years or more.

One may conclude from this study that while transplantation of the ureters to the bowel is not a perfect operation in the physiologic sense, it does offer a great measure of relief from an otherwise very distressing situation. It has shown that the life expectancy of persons with an exstrophic bladder is increased measurably by suitable treatment and that their subsequent lives may be nearly normal. It has shown that the major problem in the subsequent treatment of such patients is the control of pyelonephritis, and that the pyelonephritis is most frequently accompanied by obstructive phenomena. The advent of the newer chemotherapeutic agents and antibiotics may do much to reduce the disability thus incurred, but it will not answer the whole problem.

The Results of Diathermy Treatment of Villous Papilloma of the Bladder. HUGH DONOVAN. *Brit. J. Urol.*, 1950, 22: 322.

The author discussed diathermy for papillomas of the bladder chiefly from the standpoint of the physical properties of the high frequency electric current employed in their destruction. Attention is called to the fact that the destructive effect of the current used in diathermy is produced by the heat generated by the resistance to the passage of the current through the tumor.

The danger of electrocution passes when the current is operating (oscillating) at more than a half million cycles per second. Roughly speaking, "coagulation" current is generated at about 3,000,000 cycles per second, whereas "cutting" current is nearer to 5,000,000 cycles per second. The explanation for this is that cutting is achieved "by the blow of the arc; such an arc appears to absorb a great deal of energy and, therefore, the heating-through effect on the tissue is greatly lessened."

The author described some experiments used in an effort to determine the depth of destruction of a papilloma by fulguration. He concluded that the depth is less than 3 or 4 mm., even though the fulguration is prolonged and the voltage increased. Determinations were made also on the relative effectiveness of distilled or other varieties of water as an irrigating agent during fulguration. The conclusions reached were that "current which flows is smaller when the fluid in which the tissue is immersed has very low conductivity (namely, tap water and distilled water), but the percentage depth heating is greater with distilled water; there is a moderate fall-off with Birmingham tap water, and a still bigger difference for hard water."

The problem at hand, therefore, is the adequate removal of the bulk of the tumor so that only a thin layer is left for fulguration. The author mentioned the use of repeated fulgurations at intervals of about 6 weeks, to allow enough time for the destroyed tissue to slough away. He also mentioned the removal of the bulk of the tumor before fulguration with forceps or a resectoscope. He emphasized the fact that if these limitations of the diathermy current are not taken into consideration, the results of this form of treatment will be disappointing.

JOHN L. EMMETT, M.D.

Results of Treatment of Bladder Papilloma by Diathermy, from the Western Infirmary, Glasgow. JOHN H. MCBEATH. *Brit. J. Urol.*, 1950, 22: 376.

This is a brief summary of 243 cases of papilloma of the bladder in which treatment was administered at the Western Infirmary, Glasgow, between the years 1922 and 1945. Of the 243 patients, 158 (65 per cent) were treated by diathermy (fulguration). Cystoscopic fulguration was used in lesions no larger than "the terminal phalanx of the thumb" or for multiple smaller lesions (less than 12 in number). Suprapubic fulguration was used for larger or more numerous lesions. Most patients who had lesions which could be treated cystoscopically were treated without anesthesia and as outpatients.

In order to evaluate the results, the lesions were divided into groups designated as simple (benign?) lesions and malignant lesions. There were 120

simple, and 38 malignant, lesions. Only 78 of the 120 patients with simple lesions could be traced, whereas all of the 38 with malignant lesions were traced. Sixty-nine of the 78 patients with simple lesions survived more than 5 years, many of these being known to survive from 10 to 20 years. Of the 38 patients with malignant lesions, only 11 survived more than 5 years.

An investigation into the incidence of "daughter" tumors or vesical recurrences did not show any correlation with the ultimate prognosis.

JOHN L. EMMETT, M.D.

A New Method of Immediate Closure of the Bladder (Un nuovo metodo di chiusura immediata della vescica). Th. HRYNTSCHAK. *Urologia*, Treviso, 1950, 17: 201.

The procedure for immediate closure of the bladder used by the author is easy to learn and any young urologist can apply it with good results after a short period of training; personally, the author has always obtained satisfactory results since he began to use the procedure about the end of 1948: of 96 patients operated upon and followed-up, 1 developed a bladder fistula, in 83 the catheter was definitely removed during the first 5 days after operation, and in the remaining 12 patients it was removed between the sixth and the fourteenth days.

The method consists of a tobacco pouch suture involving the bladder musculature. In the preparation of the bladder it is particularly important to detach the peritoneum and to reattach it as highly as possible so that the bladder wall is widely freed. All the perivesical tissue, and especially the fat tissue, must be well pushed peripherally in this circular area, to leave the bladder musculature completely denuded. The area to be freed must have a diameter of from 4 to 6 cm. and be nearly circular in shape. The bladder is always opened bluntly and, as far as conditions permit, transversely. The farther the opening of the bladder is kept from the space of Retzius, the easier and the more solid and rapid will be the repair.

With an ordinary round needle holding a long, strong catgut suture, the author perforates the bladder muscle as deeply as possible, without picking up the mucosa, at a distance of 7 to 10 mm. from the edge of the wound at predetermined points; generally, five bites are taken with certainty that enough room is left between the sutures to allow introflexion of the muscular wall. The sutures are tied slowly and energetically while the assistant attends to introflexion of the vesical wall. Impermeability of the suture line is verified through a previously introduced urethral catheter, with 100 c.c. of physiologic salt solution and from 100 to 150 c.c. of air. This method provides a true valvular closure. The center of the suture is reinforced with a typical Z suture; if air escapes from the wound during control, a Z suture is applied over the defect.

The patient is allowed to rise the day after operation and to urinate spontaneously. The abolition of the catheter, or its use for only a minimal time, not only avoids infection of the urine but also contributes to rapid healing of the wound. All patients are given 1 million units of penicillin during the first 5 postoperative days. RICHARD KEMEL, M.D.

Paraffinoma of the Penis: Case Report. ROBERT H. BRADLEY, JR., and WILLIAM A. EHRGOTT. *J. Urol.*, Balt., 1951, 65: 453.

Paraffinomas are tumors resulting from the presence of paraffin or mineral oil in the tissues. The tumors were first recognized 40 years ago, following the use of paraffin in 1899 by Gersuny. They were first described in 1906 by Heidingsfeld and the term paraffinoma was applied to them in 1913 by Benedek.

All of the tumors show the same pathologic picture; a connective tissue new growth resembling a granuloma containing a series of oval or round cavities like Swiss cheese, filled with oily matter. Macrophages and giant cells are present, but caseation is rare. The growths develop in from 6 to 15 months after the introduction of the paraffin. Masses of varying size appear in the subcutaneous tissue attached to the epidermis. They are bluish red, brownish red, or pale. The vessels of the overlying skin are distended and fill slowly after pressure. Disfiguration is marked.

Tumors do not always develop following the injection of paraffin. Differences in reaction may be due to varying degrees of purity of the oil, but apparently the determining factor is sensitivity of the patient's tissue. The use of nose drops with an oily base has been condemned with the recognition of lung paraffinomas following their use. Recently it has been shown that significant amounts of mineral oil taken by mouth as a laxative may reach the lung, and that this accounts for nearly half the adult cases of oil respiration pneumonia. In cases of diverticulosis of the large bowel, the regular use of mineral oil may cause paraffinoma formation in the mesenteric lymph nodes. Cases of tumors are reported following the use of high pressure grease guns by malingerers trying to avoid military service and attempting to enlarge the penis by the subcutaneous injection of paraffin or vaseline. Only 2 cases of malignant degeneration of a paraffinoma are on record.

The authors report a case in which the patient applied petrolatum and a gauze bandage to an abrasion of the foreskin of the penis. Daily dressings were used for 6 months. Four 4 ounce bottles of petrolatum and 1 small tin of icthyol ointment were used. The skin of the prepuce would heal and then break down again. Ammoniated mercury ointment, hot soaks, and penicillin were of no help. He worked with oil as a machinist and occasionally developed oil acne after marked exposure.

Physical examination showed the penis to be enlarged to twice the normal size with a hard, fixed, nontender subcutaneous thickening. The mucocutaneous junction of the prepuce was cracked and slightly infected. The glans penis was uninvolved. Bilateral rubbery inguinal nodes were present. A

biopsy of the skin of the penis and a lymph node were taken; the wounds failed to heal. Surgery involved dissection of the entire subcutaneous tissue of the penis to Buck's fascia with circumcision. The penile skin was pulled back to form a full thickness graft. One area of infection healed with antibiotics.

Various fat stains were used in attempting to identify the oil. Scarlet R showed an affinity for the vacuoles. Osmic acid showed no results, which indicated that the oil was not a neutral fat. A saponification procedure was done and the number of the oil from the specimen was 9. Human fat showed a saponification number of 118. Infrared spectroscopy showed the oil to be a saturated paraffin hydrocarbon and, therefore, mineral in origin.

It is likely that the tumor was caused by a combination of the petrolatum and the cutting oils used in the patient's work. Cutting oils are essentially emulsifying agents and are therefore water miscible. These would favor penetration of the petrolatum into an abraded skin. The patient admitted that his hands were very apt to be covered with oil when he went to urinate while at work and that his overalls were often saturated with cutting oil.

NATHAN ROSENBLOOM, M.D.

GENITAL ORGANS

The Hormonal Nature of Prostatic Hypertrophy as Deduced from Histopathologic Data and Analyses of Comparable Findings in Certain Hyperplastic-Dysplastic Affections of the Female Breast (Sulla natura ormonale dell'ipertrofia prostatica attraverso i dati istopatologici e l'analisi comparativa con alcune affezioni iperplastico-displastiche della mammella femminile). A. FERRARA, F. DESTRO, and G. PICCOLO. *Arch. ital. urol.*, 1950, 24: 247.

Six operatively removed (fresh) specimens of prostatic hypertrophy were studied histopathologically. The findings were then compared with those of 12 specimens of fibroadenoma and 3 of pure adenoma of the female breast, and, finally, with 5 specimens of Reclus' mastopathia. There were also examined for controls 3 prostate glands and 3 breasts of normal adults, 1 breast of a female adolescent, and 1 breast of a woman in the puerperium. The following histologic tests (hematoxylin-eosin-orange, Mallory, van Gieson, Unna-Taezer-Livini, and Goemori) were used to demonstrate the most common structural components of the tissues: the muscular, elastic, and argentophile components.

Instead of detailed descriptions of the cellular morphology, a series of photomicrographs are appended to the original article; they show not only the most pertinent structural details but also illustrate the most important comparative findings between the various normal and abnormal specimens, and, particularly, the comparative histology of the hypertrophic prostate gland and of Reclus' disease.

The similarities between prostatic hypertrophy and Reclus' affection—an affection on an admitted hormonal basis—are most striking. The photomicrographs show the same early solid budding of epithelial tissues with subsequent cavitation of the buds, the latter eventuating in a cavity lined with a double row of cubical epithelial cells or in a cystlike development with a single row of flat lining cells. There is the same paucity of stromal reaction (estrogenic effect), and in this regard the authors believe that the previous reports of a fibromyomatous form of prostatic hypertrophy are based on two fundamental errors—the first error originating in the material, which in these early studies came exclusively from autopsies (was not fresh), and the second, in the incorrect diagnosis, which did not distinguish between true prostatic hypertrophy and the connective tissue hyperplasias of chronic infective and phlogistic processes.

Another similarity between prostatic hypertrophy and Reclus' affection lies in the cellular dysplasia: the epithelial cells assume an abundant cytoplasm, become highly cylindrical, and reveal inclusions (lipid granules and vacuoles) which may proceed in both conditions to the appearance of functional activity.

A clinical resemblance of both conditions lies in their tendency to appear late in life, at a period when disturbances in the hormone balance become most pronounced. These hormonal disturbances have been vastly discussed in the medical literature, but in the authors' opinion, the etiopathogenesis of prostatic hypertrophy must still remain a matter of speculation. This much they believe has been established: that true prostatic hypertrophy is based on hormonal disturbance or imbalance and that the glandular epithelium per se is the constituent involved in the hyperplastic stimulus (androgenic effect).

These studies have shown that the internal sphincter of the bladder neck does not take part in the formation of the so-called capsule; the capsule is formed by the submergence of, and peripheral pressure on, the normal prostatic stroma by the exuberating glandular epithelial tissues.

Special examination of the so-called periurethral glands in prostatic hypertrophy shows that these glands tend to be pressed out themselves instead of proliferating and pressing the entire rest of the gland peripherally to form the so-called capsule. The photomicrograph of this area shows merely a few glandular structures buried in a dense mass of sclerotic tissue.

JOHN W. BRENNAN, M.D.

Experiences with Prostatectomy by Henrikson's Method. ARNE HOMB. *Acta chir. scand.*, 1950, 100: 597.

Although the author reviewed 354 cases of prostatic hypertrophy treated during a 4 year period in one of the Norwegian hospitals, this study was primarily a consideration of an unpublished operative technique proposed by Henrikson.

The original operation has been designated "Henrikson's Method II" and consists of exposing the

prostate through a blunt transverse opening at the level of the bladder neck. The adenomas are enucleated through this aperture, which retains many of the features of a muscle-splitting incision. The bladder is drained by a long rubber tube with 3 holes in the midportion, which is placed through the urethra and is brought out through a stab wound in the vertex of the bladder. The bladder neck is closed in three layers and a small pack is placed over the suture line. Bladder irrigations are avoided and on the third or fourth day the suprapubic segment of the drainage tube is cut off and the remainder is used as an indwelling urethral catheter. On or about the seventh day, the remainder of the tube is removed from the bladder and urethra.

The author modified Henrikson's operation by making a large enough opening in the bladder neck to insert retractors and control the bleeding with sutures, by using continuous irrigations for 3 or 4 days and by employing a drainage tube instead of a pack outside of the prostatic capsule.

Two groups of patients were reviewed in considerable detail. The patients in the first group were treated in the period from November 1, 1945 to October 31, 1947, and those in the second were treated in the period from November 1, 1947 to October 31, 1949. During the first of these periods, suprapubic prostatectomy (by the Freyer technique) had been the operation of choice, while during the second 2-year period most of the patients were treated by the Henrikson method.

Careful study of the two groups regarding age, residual urine, and the chemistry of the blood showed that they were comparable. During the second period, however, only 11 patients had been discharged after simple cystostomies, while during the preceding 2 years 31 had been treated in this manner.

The mortality after the Freyer type of suprapubic prostatectomy had been 10.4 per cent in 77 cases, while the Henrikson operation resulted in a mortality of 2.2 per cent in 136 cases. Although a few fluctuations in postoperative complications were noted, there were no significant differences in the 2 series. Thromboembolism continued to be the greatest problem after both types of procedures.

After the Freyer operation the patients averaged 17 days of hospitalization and the wounds were dry after an average of 26 days. After the Henrikson operation hospitalization averaged 11 days and the incisions were healed on the twelfth day.

The author concluded that this new type of prostatectomy for benign hyperplasia is especially suited for general surgeons who have had no special training as urologists. ORMOND S. CULP, M.D.

Periostitis Pubis Following Prostatectomies. GUNNAR HEY. *Acta chir. scand.*, 1950, 100: 607.

After brief consideration of approximately 50 cases of osteitis pubis reported in the literature, the author presents 15 new cases in detail. The diagnosis was made from the characteristic adductor spasm as well as the pain in the adductor muscles, and was verified by the typical bone changes demonstrated in roentgenograms of the pubis.

The patients were divided into 2 basic groups: (1) 42 who had follow-up examinations after the Freyer type of suprapubic prostatectomy, and (2) 33 who were studied after undergoing Millin's retropubic prostatectomy.

Osteitis pubis was noted in 14.3 per cent of the first group, and in 27.2 per cent of those who underwent retropubic prostatectomy. The first group had been followed for 5½ years while the second group had been followed for only 1½ years. Symptoms of osteitis pubis appeared from 14 days to 6 months after operation, but were most common during the third postoperative week.

Special attention was directed to the fact that no similar cases were noted after simple cystostomy or cystolithotomy.

All degrees of the condition were noted. Some patients had very little disability, while others had severe symptoms and were bedfast. The author insists that the risk of osteitis pubis increases from a minimum after cystostomy to the maximum after Millin's operation.

The symptoms and pathologic anatomy are considered, but it is pointed out that the etiology remains unknown. Millin's contention that this complication is due to injury to the symphysis has not been accepted by the author. The latter believes that infections in the space of Retzius have contributed most to the pathogenesis.

Streptomycin and dihydrostreptomycin were especially efficacious in the treatment of this series of infections and have been recommended as the treatment of choice.

Adequate prophylactic measures include operation while the urine is sterile, avoidance of unnecessary instrumentation, limitation of postoperative irrigation to the minimum, prompt removal of drains, the placement of all drains and tubes at some distance from the pubis, and gentle handling of the tissues.

ORMOND S. CULP, M.D.

Functional Results Following Transurethral Resection and Retropubic Prostatectomy. H. C. ROLNICK and M. A. ROBBINS. *J. Urol.*, Balt., 1951, 65: 408.

The authors report the functional end results following transurethral resection and retropubic prostatectomy in benign prostatic hyperplasia. They note that the mortality from prostatic surgery has reached an almost irreducible minimum with the improvements in technique, chemotherapy, and better anesthesia. Bleeding has been well controlled, both in immediate and in secondary hemorrhage; in this respect the resectoscope has been of superb aid. Similarly, morbidity is not the very great problem that it was in the past. After transurethral resection, the patient leaves the hospital more quickly than after the other methods; however, the period for recovery is as long as after open operations,

if not longer in many cases. Many months often elapse before the frequency and pain on urination subside. Thus, the authors are now concerned with the functional end results of surgery, rather than with merely the mortality and morbidity. The various approaches to the enlarged prostate gland should be known and should be used as required by all qualified urologists, as each type has an occasional superindication.

The discussion concerns 150 patients subjected to transurethral resection and 24 subjected to retropubic prostatectomies who were observed over periods ranging from 3 to 14 months postoperatively; all of them had had benign bladder neck obstructions. Of 79 from whom 20 or fewer grams of tissue had been resected, 59 showed definite improvement in the condition. Twelve others had symptoms lasting from 3 to 12 months, which finally cleared with local treatment. Ten others had poor results requiring secondary resection; among these were included cases of re-contracture of the bladder neck following the resection. Of 49 patients with glands weighing more than 20 grams, 40 presented good results and 9 presented fair or poor results. This gave an over-all picture of 107 who were benefited and 32 whose condition was the same or worse after surgery. Some of the patients complaining of pain and frequency presented negative cystoscopic findings and the prostatic urethra appeared to be well resected. It is interesting that patients with the smaller glands gave a poorer functional result than those with the larger hypertrophies; it is commonly agreed that transurethral resection is best indicated for the smaller glands.

Four patients requiring re-resection had so-called "neurogenic bladders," while the 6 others had large hypertrophies and remaining tissue.

Two patients showed temporary incontinence; in 1 it lasted for 3 months while in the other it lasted 1 year. Both have good control now.

Meatotomies were done whenever necessary. Urethral strictures following resections were, of course, not uncommon; they are due, in the main, to overdilatation with the No. 28 instrument, to the to-and-fro motion of the instrument, to the inability to keep the sheath lubricated, and to the possibility of some heat conduction by the bakelite sheath. The authors noted that attempts to keep the sheath well lubricated were not too successful. The method suggested by Nesbit for external urethrotomy in small caliber urethras was used in 3 cases.

The greatest problem has been the postoperative bladder neck contracture. The authors believe that the spark gap method of coagulating causes much more charring and thermal penetration than the tube current; they disagree with Weyrauch, Bassett, and Berger in this matter. They note the extreme leathery feel of the resected area following spark gap coagulation in the patients requiring prevesical drainage for extravasation. When the tube machine was used, the prostatic bed felt soft, as one would find it to be following open surgery.

In several patients who had had a previous resection, cystostomy for tumors showed a hard, rigid, and fibrotic bladder neck; this had occurred despite wide resection of the neck, both initially and for the relief of contracture. It was noted that in choosing patients for resection, none with borderline or questionable types of possible bladder neck obstruction was operated upon; these were the particular ones which had considerable trouble later and in whom the symptoms were markedly aggravated following resection. Apparently a burn or scar is superimposed on the previously engorged and inflamed tissue.

The authors suggest cutting a wedge from the contractures rather than resecting a wide circular area. Perhaps the perfection of the tube current would aid in preventing contracture.

The end results of retropubic prostatectomy have been impressive. Bleeding is well controlled during the time of surgery, and bag catheters are not usually required. There is little fever, the patient heals faster, and the urine becomes clear more rapidly. In 2 patients there was slight tenderness over the symphysis; the condition cleared up within 3 weeks. The patients were not disabled and presented neither clinical nor roentgenological evidence of osteitis pubis. The functional results were uniformly good, except for 1 contracture which necessitated transurethral resection of the neck; the end result was good. Two of the 24 patients required fulguration with the resectoscope for secondary bleeding.

The questions raised by the authors as to the reasons for the complications following resection and the possible solutions are most enlightening.

NATHAN ROSENBLOOM, M.D.

MISCELLANEOUS

Urological Survey of Anuria and Oliguria with a Guide to Treatment. FRANKLIN FARMAN, KENNETH A. LEMON, and HAROLD L. BRISKIN. *J. Urol.*, Balt., 1951, 65: 177.

The urologist's conception of renal failure characterized by oliguria and anuria requires revision, according to the authors.

The three leading morphological factors in the pathogenesis are: (1) vasospasm of the interlobular arteries and arterioles supplying the glomerulus and tubules, leading to diminished glomerular filtrate, (2) alterations in the function of the proximal tubules, and (3) blockage of the distal tubules or back pressure from obstruction of the lower urinary tract which leads to alteration in the epithelium.

Vasoconstriction of the arterioles and blockage of the distal nephron and lower urinary tract are most amenable to treatment. Whether damage of the proximal tubule is reversible depends upon the severity of the toxic factor and, as in all causes, upon the recognition of the factors and early institution of proper treatment.

Renal failure may occur in association with the following conditions: pyelonephritis, the crush syndrome, sulfonamide sensitivity, intravascular hemo-

lysis, hemoglobinuria, prolonged shock, toxemias of pregnancy, lower urinary tract obstruction, burns, heat stroke, poisoning (especially with heavy metals), acute gomerulonephritis, infectious hepatitis, biliary tract operations, infantile diarrhea, and any diseases causing excessive vomiting and alkalosis, to list but a few.

A variable degree of shock is frequently found early. Rising azotemia, moderate hypertension, vomiting, edema, proteinuria, hemoconcentration, abnormal electrolyte levels, and oliguria or anuria are frequently present, but variable. The urine in oliguria is frequently highly acid with low fixed specific gravity and a smoky appearance during the first days.

With the urinary output below 600 c.c. per 24 hours and the presence of one of the known etiological factors, the possibility of renal failure must be considered. The management in the initial phase is the treatment of shock by transfusion of whole blood or washed red cells. Morphine or procaine given intravenously is frequently valuable in the release of the neurogenic influence. Daily determinations of the blood urea, sodium, chloride, and carbon-dioxide-combining power are begun. Fluids are administered only in the quantity necessary to replace fluid loss.

From 600 to 1,000 c.c. of fluid per 24 hours are lost by the way of the lungs and skin. Any fluid loss in addition, as in vomiting, can be measured. In the presence of vomiting, fluids can be given through a gastric tube including the return of all vomitus. This assists in controlling the water balance and replacing the electrolyte loss. Severe acidosis is treated either with sodium bicarbonate or by the intravenous administration of 1/6 m. sodium lactate or Ringer's solution. Until the onset of diuresis when chloride is excreted in large amounts, it is unlikely that there would be need for further electrolyte therapy. A protein-free diet which is high in carbohydrates and fat should be given with the aim of maintaining a high caloric intake and suppressing nitrogenous breakdown. Until the onset of diuresis, which may be expected in 5 to 10 days, supplementary measures may be necessary to combat the progressive azotemia. Such measures as gastric lavage or intestinal perfusion are simple, whereas peritoneal dialysis or artificial kidneys are more elaborate but may be more effective. Renal sympathectomy is advocated by some to counteract cortical ischemia and cellular anoxia resulting from paravertebral or spinal anesthesia, or renal decapsulation.

The authors have divided their 35 cases of anuric uremia into 9 cases of acute nephrosis of the upper nephron with an 89 per cent mortality, 18 cases of acute nephrosis of the lower nephron with a 61 per cent mortality, and 8 cases of acute glomerulo-arteriole vasoconstriction with a 62.5 per cent mortality. Chronic renal disease was associated in 24 cases with a 75 per cent mortality.

HERBERT J. KAROL, M.D.

Serum Albumin in Uremia: A Clinical Investigation Correlated with Reversible Uremia in Dogs.
ROGER BAKER. *J. Urol.*, Balt., 1951, 65: 197.

Basic and fundamental information about the abnormal physiology of uremia is still lacking. In order to permit study of a selected degree of uremia and reversal of the same, a benign and practical procedure was used in which, by tension on a Penrose drain inserted under a small mobilized section of the distal ureters, uremia could be induced, and by release of this tension, it could be reversed.

Investigation required qualitative as well as quantitative determinations of serum albumin. The quality depends upon the phenomenon that certain molecules have an affinity for serum proteins. Attraction between the negative-charged molecules and the positive-charged serum protein results in binding the molecule to the protein. Departure from the normal measurements indicates abnormal protein.

Phenolsulfonphthalein (PSP) is adsorbed to serum albumin and the amounts are dependent upon the quality of the albumin. The binding index is a measure of the quality of the protein and this equals $\frac{\text{u. gm. of PSP bound}}{\text{albumin gm. per 100 c.c.}}$. The quantitative protein analysis was determined by Howe fractionation and the nonprotein nitrogen by the Folin-Wu method.

Progressive weakness, apathy, and stupor were noted in the 5 dogs used in the experiment. Fluid and food intake was well maintained. The urinary output was normal on the average of 48 hours after the release of the tension on the ureters. When a dog was made uremic the second time, the condition was tolerated better. The PSP binding index (BI) of the dogs in uremia was decreased on an average of 41.6 per cent and was proportional to the elevation of the nonprotein nitrogen (NPN). With termination of the uremia, both the NPN and the BI returned to normal. The greatest decrease in the BI occurred in the dogs in which uremia was produced for the second time and occurred irrespective of minor variations in the NPN.

Twenty-five cases of uremia in human beings were studied. These consisted of 12 cases of urinary obstruction, 3 of glomerulonephritis, 3 of lower nephron nephrosis, 3 of arteriosclerosis, 2 of nephrosclerosis, and 1 case each of polycystic kidneys and atrophic pyelonephritis. The age range was from 8 months to 87 years.

The normal mean BI was 57. In uremic patients the BI decreased about 53 per cent in each case of uremia regardless of the etiology. The variations of the BI did not follow the clinical signs and symptoms but were proportional to the NPN. Neither sex nor age had any effect.

Because of the decrease in the BI of the PSP in human beings with uremia, an altered albumin was present. Although the clinical signs and symptoms may not indicate the true severity of the uremia, the BI and NPN do so despite the age or etiology.

The speed with which the abnormality of the protein develops and the normal basic composition of

the molecule preclude any fundamental defect. In uremia the loci of attachment normally occupied by PSP are unavailable, which causes the decrease in dye attachment. The most acceptable possibility is that another molecule may be bound by serum albumin. Increased concentration of NPN per se does not apparently act directly on albumin to produce the abnormality present in uremia. The possibility exists that in uremia the increase in NPN produces fatty degeneration of the liver which elaborates a fat or lipid bound to albumin and causes the decreased BI.

Serum from uremic patients was extracted with ether by McFarlane's method, and, in 2 cases studied, there was a 26 and 40 per cent increase in the BI of PSP. An ether soluble compound, most probably a lipid, was apparently removed, and, as a consequence, there were more available loci on the albumin for binding by PSP.

HERBERT J. KAROL, M.D.

Osteitis Pubis. ERNEST F. HOCK and KENNETH A. KURTZ. *J. Urol.*, Balt., 1951, 65: 419.

Osteitis pubis has become more common with the advent of retropubic prostatectomy. The authors noted 3 cases after 29 retropubic operations. The pathogenesis is still unknown. Infection in the prevesical space has been blamed, but Rosenberg and Vest, in 3 cases, and Kessler, in an autopsied case, found no infection. Wheeler pointed out the many features in common with Sudeck's bone atrophy.

The authors reviewed 31 cases of osteitis pubis and 2 cases of osteitis of the spine reported in the literature. These occurred as follows: 8 cases following transurethral resection, 13 following two-stage prostatectomy, 4 following one-stage prostatectomy (suprapubic), 4 following retropubic prostatectomy, 1 case following abdominoperineal bowel resection for carcinoma, 1 following perineal prostatectomy, 1 following ureterolithotomy, and 1 following severe Bacillus coli pyelonephritis, a nonoperative case. The last 2 cases occurred in females. Various organisms were cultured in the urine. An average of 6 weeks elapsed before roentgenographic changes were seen. Four patients had a suprapubic draining sinus. Therapy in general was unsatisfactory. The average duration of the condition when first seen was 3.5 months. The features common to all cases were:

1. Infection of varying severity with poor antibacterial response.
2. The onset was usually sudden, beginning weeks or months after surgery.
3. The pathological process was primarily atrophy, rather than inflammation of the bone.

The authors tentatively believe that the mechanism is similar to that of Sudeck's atrophy. Probably a chronic inflammatory process within the pelvis may cause irritation of the sensory nerves, which, through a causalgialike mechanism, leads to pain, ischemia, muscle spasm, and trophic changes. The chronic low-grade inflammation has a "sensitizing" effect, which if followed by any additional stimulus may produce a causalgia. The authors theorize that since the prostate and capsule have a very rich sensory nerve supply, incision of the anterior capsule (as in the retropubic technique) would cause pain to be referred anteriorly to the pubic and adductor regions. In the suprapubic approach, there is frequently backache, sciatica, and arthritis, due probably to trauma to the posterior and lateral lobes of the prostate. This might explain the cases of osteitis of the spine following prostatectomy.

Treatment should consist of (1) removal of the focus of irritation, i.e., infection, and (2) interruption of the noxious reflex. The authors, following the work suggested by Grace, have used a diffusing agent in combination with the antibiotics; aqueous zephiran was used. In 1 case, following cystostomy, infection, and transurethral resection, a large urethral stricture was found. In the vesical neck region the urethra was smooth, pale, and indurated. Six cubic centimeters of 1 per cent novocain were injected into the prostatic capsule at the vesical neck and in the area of several tags. The area was scarred and much pressure was needed to inject the solution. Much relief was felt in several minutes and the patient was able to walk erect without his cane.

In a second case, following retropubic prostatectomy and orchectomy for carcinoma, an adductor spasm developed following infection of a suprapubic sinus. Nupercaine solution (¼%) injected into the sinus caused temporary relief. Etamon (300 mgm.) given intravenously also produced temporary relief. Finally, the injection of novocain into the anterior prostatic capsule produced relief in 5 minutes and it persisted. One repeat injection was done for further permanent relief.

A third patient had a pyocyanic infection following a retropubic prostatectomy. This healed with chloromycetin given by mouth. Osteitis pubis occurred 30 days after surgery while the patient was at home. Again the local injection of novocain into the ananterior prostatic capsule gave marked and sudden relief.

A fourth case, showed relief with ¼ per cent nupercaine solution injected into the bladder. The infection was cleared with streptomycin for a Bacillus pyocyaneus infection.

The case reports seem to indicate that the authors' concept of the pathogenesis of osteitis pubis is basically correct. Both the infection and the trigger mechanism for the reflex must be treated.

NATHAN ROSENBLOOM, M.D.

Perforation of the Upper Urinary Passages by Calculus (Perforazione da calcolo delle vie urinarie superiori). ENRIQUE PÉREZ CASTRO. *Urologia*, Treviso, 1950, 17: 208.

The author reports 3 cases of perforation of the upper urinary passages by calculi. In the first, the patient had had hematuria for many years when she walked too much and, on the occasion of a left lumbar traumatism, developed intense pain which re-

quired analgesics and gradually disappeared. One year ago an abscess had formed which opened spontaneously at the left iliac crest, and some time later a small calculus was found when the dressing was changed. The left kidney was functionless and contained a calculus reproducing the pelvis and calyces. The lower pole of the kidney presented a mass of concretions and the drainage tube reached close to this mass. Subcapsular nephrectomy was done and the postoperative course was normal. In the second case, in which left nephrectomy had been performed for renal calculosis 1 year previously, the point of an irregularly shaped calculus had perforated the right renal pelvis. The opening was enlarged, the calculus extracted, the renal pelvis closed, and the region drained through a lumbar tube. In the third case a calculus wedged in the right renal pelvis had caused an enormous hydronephrosis with rupture of the lower pole of the organ, necessitating nephrectomy.

The author gained the impression that the calculous sclerolipomatosis was more developed in his cases than in those of other countries: while he observed only slight or no perirenal reaction to renal calculi in Germany, he usually found tenacious adhesions in Spain, which made isolation of the kidney very difficult; this may have been connected with the factors of living and race of the patients. When renal perforation occurs early or before the perirenal tissues present phenomena of sclerolipomatosis, urinary infiltration meets no obstacles to its spread, as in Everett's case of direct erosion of the lower pole of the kidney caused by a coral-shaped calculus on the occasion of an effort by the patient. Thus, in perforations of hydronephrosis caused by complete occlusion through wedging of a calculus, rupture of the greatly thinned parenchyma is much easier when there is no inflammatory infiltration of the wall, as in the third case. It must not be forgotten that spontaneous repair of the kidney perforated by a calculus is possible, and that death of the organ does not necessarily follow if the latter was in good functional and anatomic condition before the accident occurred. There is also a natural tendency to occlusion of the perforation through which the calculus has escaped into the neighboring tissues.

RICHARD KEMEL, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Single or Multiple Infarcts of the Bone in the Adult as a Result of Aseptic Vascular Obstruction (Infarctus unique ou multiple des os chez l'adulte, résultat d'une obstruction vasculaire aseptique.) DALLAS B. PHEMISTER. *Presse méd.*, 1950, 58: 1430.

The author reviews the work of Kienboeck and of Axhausen on the aseptic necrosis of bone following trauma of the vascular supply to this bone. Two hundred cases of aseptic infarcts of bones have been reported in the past 15 years as well recognized sequelae of occlusion of the blood vessels to these bones. These cases are almost equally divided between those due to caisson disease and those caused by vascular occlusion of obscure origin.

The first cases reported by the author in 1939 and in 1940, due to caisson disease, are reviewed in detail. The first case was diagnosed 4 years after the occurrence of caisson disease. This was proved by biopsy of the head of the right femur, which showed the typical pathological changes. The second case was proved at autopsy following death of the patient, at the age of 60 years, from carcinoma of the lung; this patient had suffered from caisson disease 34 years previously. A full pathological description is given. Since the publication of these cases, several cases dating from 3 to 22 years following caisson disease have been studied.

Reports of the study of 3 cases of infarcts in the long bones due to vascular occlusion of unknown cause are given. These cases are characterized by a more insidious onset than those caused by caisson disease.

More profound studies are necessary to classify the etiology of vascular occlusion in the cases of single and multiple infarcts of bone. The systematic examination of the long bones at autopsy will reveal unexpected lesions and their study could lead to important bacteriologic and pathologic discoveries. Likewise, systematic roentgenography at autopsy will reveal the presence of many infarcts which are not suspected. THOMAS C. DOUGLASS, M.D.

Clinical, Radiologic, and Histologic Considerations on Familial Poliostotic Osteodystrophy (Consideraciones clinicas, radiologicas e histologicas sobre osteodistrofia poliostotica familial). MANUEL RIVEROS, QUIRNO CODAS THOMPSON, and JUAN BOGGINO. *Rev. ortop. traumat.*, B. Air., 1950, 20: 1.

The authors describe 4 cases of familial poliostotic osteodystrophy, a peculiar disease which occurs in females and shows a predilection for the maxillary bones. These cases were observed in a family of 10 members belonging to two generations.

The disease began in infancy and, with some modifications, persisted during the whole life of the patient, involving especially the facial block and particularly the maxillary bones. The lesions were deforming and produced the aspect of the fat-cheeked cherubs of classic religious paintings; hence, the name of "cherubism" proposed by Jones. The maxillary changes displaced the teeth and made them fall out, simultaneously imparting an ogival shape to the hard palate. The disorder was accompanied by a reaction of the submaxillary ganglions, at least during the first years, which disappeared later in the adult. Calcemia was elevated in 2 cases and below normal in 1 case.

Roentgenologically, the disease was manifested by a multilocular cystic process located prevalently in the maxillae and it presented a characteristic picture that consisted of multiple cyst formations with gross partitions, inflammation of the bone where the process came in contact with it, destruction of the spongy bone by tumoral growth and of the alveolar process which caused luxation and falling of the teeth without periosteal reaction or bone condensation, also deformity of the maxillary and mandibular bones, and even elevation of the orbital floor with exophthalmos.

In 1 case changes were also found in the multangular bones of the carpus on both sides, and the classical picture of soap bubbles was seen on the left side. In another case with localization in the maxillae and mandibles, the polycystic aspect was well marked in the pyramidal portion of the maxillae, with deformity of the orbital floor and the external wall of the maxillary sinus. Localization in the mandible deformed the bone with increase in the trabecular density and also of the compact bone in some areas. A porotic lesion was observed in one of the right maxillae.

Histopathologically, the lesion seems to evolve in two stages: osteoclasis followed by osteosis without the formation of normal bone. The lesion is always destructive and productive, the destructive activity predominating in the beginning and the productive activity later.

Osseous fibrodysplasia was found in an older patient who had been observed for many years; the roentgen lesions seemed somewhat different from the others and clinically appeared to have regressed. RICHARD KEMEL, M.D.

Eosinophile Granuloma (Granulome éosinophile). CARLOS SALAZAR DE SOUSA and ABILIO MENDES. *Sem. hôp.*, Paris, 1951, 27: 33.

The authors give a very good review concerning the history of eosinophile granuloma, a still etiologically unexplored lesion. This condition was originally described by Finzi in 1920 as "myeloma of the frontal bone with predominance of the eosinophile cells." They consider an infectious origin, such as that in typhoid or brucellosis granuloma, as most

probable, which agrees with the opinion of Lichtenstein and Jaffe, who assume that a virus infection is present. Trauma as the causative factor is considered very doubtful. At the present time spontaneous healing and x-ray irradiation have made surgery unnecessary.

The histological findings are: granulation tissue, newly formed capillaries, fibroblasts, eosinophile cells, proliferation of reticuloendothelial cells, giant cells, neutrophils, and lymphocytes. Cases with multiple lesions are cited as well as such lesions with recurrences. The strictly osseous changes are more common in males and in early childhood, with predilection for the cranium, but practically every bone can be involved.

The clinical signs are not specific, and the blood picture and chemistry are normal except for an occasional increase of eosinophils. X-ray examination shows a well defined defect without periosteal reaction and decalcification. As for the differential diagnosis the following have to be considered: bone cysts, giant cell tumor, Ewing's tumor, osteomyelitis, tuberculosis, and syphilitic involvement. In case of multiple lesions, osteitis fibrosa cystica and myeloma have to be ruled out. Only biopsy can reveal the true nature of the lesion. In contrast to Lichtenstein and Jaffe, other authors attribute the lesion to one phase of xanthomatosis or to reticuloendothelial disease (Christian-Schueller). In the authors' opinion eosinophile granuloma is of benign nature with definite histologic changes. E. H. BETTMANN, M.D.

Giant-Cell Tumor of Bone; Current Status of the Problems in Diagnosis and Treatment. LOUIS LICHTENSTEIN. *J. Bone Surg.*, 1951, 33-A: 143.

Identification of giant cell tumors is not a simple matter. There is considerable uncertainty in separating true giant cell tumors from the spurious "variants" which have little in common with the true tumor. On the whole, these variants have a good prognosis and their inclusion in statistics pertaining to true giant cell tumor have caused this lesion to be less feared than it should be.

The diagnosis must not be based entirely upon roentgenography or entirely upon microscopic findings as such lesions as the nonosteogenic fibroma of bone, chondromyxoid fibroma, or aneurysmal bone cyst may closely resemble the true giant cell tumor both under the microscope and on the roentgen film. The clinical features must be used to help in the diagnosis. For instance, true giant cell tumors rarely occur in individuals under the age of 20; these tumors are located at the ends of the bones if situated in long bones, and are found much more commonly above or below the knee than in any other location in the body. When bone tumors with giant cells superficially resembling the true tumor are found in other locations or in younger individuals, the diagnosis must be viewed with some suspicion. The true giant cell tumor is a formidable lesion.

The author uses a grading system based on the degree of atypism of the stromal cells. Grade 1 shows the least tendency toward malignancy, while grade 3 appears dangerous. This grading has been useful in predicting the course of the lesion and in planning treatment.

Biopsy is indicated as a preliminary step to any type of treatment. A frozen section is satisfactory for general identification of the tumor, although grading requires good paraffin slides. These tumors should be treated by excision, resection, or thorough curettement, in accord with their location and size. Since most of these tumors are situated in the knee area, excision can rarely be done without sacrifice of the extremity.

X-rays alone appear to control certain giant cell tumors, particularly the less aggressive ones. The dosage must be adequate, but excessively high dosage may result in sarcoma after a latent period of several years during which the lesion may appear to be cured.

In recurring tumors the author recommends ablation, if this is possible, for metastases are a definite hazard. NEWTON C. MEAD, M.D.

The Malignant Tumors of the Bones with Febrile Symptomatology; Pathogenesis of Fever in Malignant Neoplasms of the Skeleton (I tumori maligni delle ossa con sintomatologia febrile; sulla patogenesi della ipertermia nelle neoplasie maligne dello scheletro). C. ZAGNONI. *Chir. org. movim.*, 1950, 34: 311.

Numerous and principally contrasting hypotheses have been advanced to explain the origin of neoplastic fever; above all it was thought to be of microbic origin, and the not infrequent finding of micro-organisms in the tumoral tissue could in part explain such a theory. The possibility that the fever is due to the anemia which accompanies the tumors is usually regarded with open skepticism, but the opinion that it is attributable to a toxic, infectious or dyscrasic factor has received more credence. The concept of neoplastic autointoxication has also been advanced. In final analysis the phenomenon could be interpreted as a reaction of the organism to the protein intoxication by the tumoral poisons which arise pathologically, enter the blood and muscle systems, and affect the physiologic, oxidative, and immunizing processes.

Among the numerous cases of bone tumor admitted to the Surgical Clinic of Padua, the author has found 17 in which the fever was probably attributable to the neoplastic factor since no other clinical cause could be found to justify the rise in temperature. Since many malignant bone tumors present an afebrile course, the problem was to find, in these 17 cases, some common characteristic which could serve as the basis for a logical explanation of their peculiar clinical symptomatology. The only common factor found was that the bone elements in which the tumors appeared consisted largely of spongy bone which is well irrigated and provided with hematopoietic pulpy tissue. It is, therefore, highly probable that, under certain favorable conditions, cellular

lysates (the pyrogenic action of which has often been reported) are introduced into the circulation in tumors of the spongy bone tissue.

RICHARD KEMEL, M.D.

Chondromatosis—Dyschondroplasia—Ollier's Growth Disturbance (Chondromatose—Dyschondroplasie—Ollier'sche Wachstumsstoerung). GERHARD EXNER. *Fortsch. Roentgenstrahl.*, 1950, 73: 454.

The existence of unilateral chondromatosis is doubted in the recent literature and the author concurs with this opinion on the basis of the following case which he has had under observation for 22 years.

A shortening of the left leg was observed during the second year of life in a girl with normal familial history. At the age of 3, roentgen examination disclosed large bimetaphyseal enchondromas in the left femur, tibia, fibula, and, later, in the fingers. However, the impressive finding was the growth disturbance in the left leg, which after 22 years resulted in a shortening of 34 cm. Further examinations during childhood revealed enchondromas in the left half of the pelvis, the ribs on both sides, and the upper left arm; the right scapula was suspicious. The disturbance in the lower left extremity together with the visible changes in the left fingers had first led to the diagnosis of Ollier's growth disturbance, but the subsequent systematic roentgen examinations of the bones showed numerous enchondromas also in the upper and lower extremities on the right side, which at first had not seemed to be involved; they were probably in part already present since early childhood. In addition, new chondromatous proliferations were also found. Thus, here was the type of polyostotic chondromatosis of the skeleton which resembles the unilateral type of Ollier's disturbance because it preferably involved the left half of the body.

The author suspects that the cases in the literature, which have been regarded as purely unilateral, would have shown similar findings later under systematic roentgen control. Worthy of note was the presence of a small hemangioma on the left nasal ala, and of several soft fibromas on the left costal arch, anal fold, popliteal region, and calf.

The disorder always starts in early childhood. The initial stages are endosseous and thus escape clinical examination. The first visible symptoms consist of nodular swellings of the bones, mostly of the hands and feet, or disturbances in the longitudinal growth of the extremities. The latter result from involvement of the epiphyseal cartilage by the chondromatous proliferations in their vicinity, and are consequently secondary symptoms. Early diagnosis is possible only by roentgen examination. On the basis of the roentgen findings a distinction is made between three stages: initial, evolutive, and involutive-regressive. Malignant degeneration may occur. In advanced stages there may be grotesque deformities of the skeleton with marked functional disturbances. In most cases the diagnosis of chondromatosis is not difficult. All attempts at an etiologic explanation of the disease have remained hypothetical. No direct familial taint has been found in most of the reported cases. The chondromatous proliferations are usually benign, but degeneration into chondrosarcoma and chondromyxosarcoma has been reported. Up till now, treatment has been symptomatic. In 1 of the author's cases the foci in the fingers were removed and bone implantation was performed with good results.

RICHARD KEMEL, M.D.

The Chemistry of the Synovial Fluid, with Special Regard to Hyaluronic Acid. LARS SUNDBLAD. *Acta orthop scand.*, 1950, 20: 105.

The author made an analysis of knee effusions in various articular disorders. The distribution of electrolytes between the plasma and fluid was in harmony with the Donnan equilibrium theory. The calcium content, however, was found to be much higher than expected, and this was explained by the fact that mucin has a calcium-binding power about ten times as great as that of serum albumin. From a biochemical point of view, synovial fluid may be regarded as a plasma dialysate containing various amounts of protein and a specific component (hyaluronic acid). The latter gives the fluid its high viscosity and thus its ability to form a lubricating film which separates the articular ends.

Degenerative as well as inflammatory conditions present a relatively high concentration of hyaluronic acid in a partly depolymerized state. The protein content is low in arthrosis deformans, moderately increased in traumatic disorders, and high in rheumatoid and infectious arthritis.

According to Inglemark and Saaf (1948) the amount of synovial fluid seems to increase when the joint bears weight, which may explain the fact that the relative viscosity in human beings is generally lower in the joints of the lower limb.

C. FRED GOERINGER, M.D.

Direct Roentgenographic Demonstration of the Nucleus Pulposus, and a Contribution to the Pathology of the Discus Intervertebralis (Direkte Kontrastdarstellung des Nucleus pulposus, zugleich ein Beitrag zur Pathologie der Bandscheibe). PETER R. ERLACHER. *Zschr. Urol.*, 1950, 80: 40.

Sixty-nine intervertebral discs taken from autopsy material were nucleographed by the author's method without the finding of a single discrepancy between the roentgenographic shadows and the macroscopic evidence. The injected fluids always remained strictly localized in the nucleus pulposus or its extensions. On the basis of these studies, 5 forms of nuclear shadow were distinguished, and the relationship of each to the development of protrusions or of prolapse is discussed.

In form 1 there is the spherical nucleus which predominates in the younger individual and seems to suggest the unlikelihood of prolapse formation. In form 2 there is the lobed nucleus which shows a few coarse pockets. The possibility of a protrusion or

eventual hernia is here left open. In form 3 there is a sample branching of the nucleus, with a shadow-in-chief in the center and only a few somewhat delicate runners extending away from the center. In this form there is at least a favorable basis for hernia. In form 4 the central shadow mass is small and the branches are plentiful and extend in various directions. In this form is found the "mixed hernia", that is, herniation of the nucleus together with parts of the annulus fibrosus. In form 5 there is no central shadow and the branches are numerous and extend in all directions. In this form there is severe degeneration; the pressure experiments fail to show any bulging or loss in height in this disc, and the formation of a hernia seems unlikely. The patients with this form are usually elderly.

Up to the present, nucleography has been carried out on 89 intervertebral fibrocartilages in 60 patients in the author's department. Various aqueous preparations of iodine have been used (contrast U, diiodon, optoiod, with preference for ioduron in 70 per cent solution). Under local anesthesia with novocain, a 10 cm. lumbar puncture needle (in part with double cannula) is inserted at the level of the upper border of the caudally following spinous process and passed in a medial and cranial direction. The interarcuate foramen is passed at its lateral angle and the needle is advanced until the resistance of the annulus fibrosus is felt. After penetrating the annulus the needle is pushed forward for not more than 1.5 cm. Here the largest practical amount of the contrast medium is injected and the roentgen exposures are taken at once. Exposures are taken from the anteroposterior, lateral, and both oblique directions.

Although no accidents have been experienced with this method, the author believes that the technique should be reserved for cases in which immediate operation is intended and in which the clinical or myelographic localization is not sufficiently exact.

In the instances in which diagnosis has been accomplished by this method, subsequent operation has fully substantiated the nucleographic findings. The author believes that the method is without danger and is worthy of further development. He has recently learned of Lindblom's work with this method, but he thinks that the perforation of the dural sac in the midline is a disadvantage.

JOHN W. BRENNAN, M.D.

Spontaneous Luxation of the Big Toe in Severe Hallux Valgus (Lussazione spontanea dell'alluce in grave alluce valgo). GUGLIELMO DE LUCCHI. *Chir. org. movim.*, 1950, 34: 273.

Among the numerous cases of hallux valgus observed at the Rizzoli Institute of Bologna, the author has never in the past 50 years seen a defect that was as serious as in the following patient. A woman of 69 had, to her knowledge, always had bilateral hallux valgus. About 30 years ago, and without particular disturbance, the medial bulge of the head of the first metatarsal had become more prominent and individualized, while at the same time the big toe became shorter and more mobile, and its original deviation corrected itself slightly. The deformity had not caused any serious disturbance as long as the patient did not take recourse to particular treatments. She had refused corrective measures.

The roentgenogram showed on the right side a hallux valgus with external deviation of exceptional degree, metatarsophalangeal subluxation, and serious displacement of the two sesamoid bones. On the left side, there were no normal articular relationships since the toe was luxated into the interphalangeal space. The base of the first phalanx was worn down medially; the head of the metatarsal was tapered. On both sides there was dorsal luxation of the second toe, and on the left side also of the third toe. The diaphysis of the second metatarsal on both sides was particularly enlarged because of the fact that the load was not carried by the head of the first metatarsal, but more laterally.

RICHARD KEMEL, M.D.

Pathological Changes of the Skeleton in Flat Feet, Based upon Surgical Explorations (Pathologische Veränderungen des Fuss-skelettes bei Plattfuessen an Hand eines groesseren Operations materials). K. NIEDERECKER. *Zschr. Urol.*, 1950, 80: 97.

Most of the pathological changes in the skeleton associated with flat feet were found in the talo-scaphoid joint. Supernumerary bones were represented by the os tibiale externum, the suprascaphoid bone, a secondary calcaneal bone, and a bipartite scaphoid. In spastic flat feet the presence of a bony block between the calcaneus and the scaphoid (calcaneonavicular coalition), and between the calcaneus and the cuboid could frequently be demonstrated. One-fourth of the 346 flat feet which were operated upon were of congenital origin. In severe cases a wedge osteotomy of the neck of the talus was necessary, but no arthrodeses are advocated and the importance of the preservation of the talonavicular joint is stressed. The talotibial and calcaneotibial ligament is hypertrophied sometimes up to 1.5 cm. For correction of the calcaneovalgus position, lengthening of the Achillis tendon and of the peroneus muscles, and partial section of the calcaneofibular and talocalcaneus ligaments are advocated. Periosteal reaction and the formation of osteophytes over the scaphoid and the talus result from the plantar displacement of the scaphoid, which, in the authors opinion, is of congenital origin; similar changes take place between the scaphoid and the first cuneiform bones. For the correction of severe forms, wedge osteotomy of the neck of the talus together with suspension of the scaphoid via the transplanted anterior tibial muscle is recommended.

Of 600 x-ray examinations, 5 per cent showed a calcaneonavicular coalition. The author's method of correction consists of a medial wedge osteotomy. After the head of the talus is temporarily removed, the bony bridge between the calcaneus and the scaphoid is separated, and the head of the talus is

put back in place. The coalition may be cartilaginous, especially in younger patients.

E. H. BETTMANN, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Impressions Concerning the Putti-Platt Reconstruction Operation for Recurrent Shoulder Dislocation. ERNEST A. BRAV and WILLIAM H. GULLEDGE. *Surgery*, 1951, 29: 82.

The various pathological changes that occur in cases of recurrent shoulder dislocations involve the capsule, the glenoid cavity, the glenoid labrum, the humeral head, and the surrounding shoulder muscle girdle.

The author emphasizes that the Putti-Platt operation produces a satisfactory barrier to continued displacement of the humeral head whether the basic defect is capsular, bony, muscular, or due to separation of the glenoid labrum.

A series of 20 cases of recurrent dislocation of the shoulder treated by the Putti-Platt method of reconstruction is reviewed. The number of patients with bilateral recurrent shoulder dislocation and the substantial proportion of patients who give no history of severe trauma associated with the original dislocation seem to suggest the likelihood of some congenital defect as a predisposing factor. The minimal limitation of external rotation resulting from the Putti-Platt method suggests that its effectiveness is not due to attachment of the subscapularis insertion to the glenoid margin, but is based on the shortening and transposition of the anterior muscle and capsular structures.

The result of the individual steps of the corrective procedure is the formation of the anterior supportive ligament by the stump of the subscapularis tendon with re-enforcement by the plicated capsular and muscle layers. A detailed description of the operative procedure is given.

A muslin bandage support in the Velpeau position is maintained for 4 weeks.

There were 19 male patients and 1 female patient. Their ages ranged between 19 and 36 years, with an average of 23.8 years. C. FRED GOERINGER, M.D.

Lesions of the Musculotendinous Cuff of the Shoulder; Some Observations Based upon the Results of Surgical Repair. HARRISON L. MCLAUGHLIN and EDWARD G. ASHERMAN. *J. Bone Surg.*, 1951, 33-A: 76.

As the result of follow-up studies on 100 consecutive patients in whom repair of the shoulder cuff was done, certain discrepancies between established theories and the behavior of the shoulder mechanism in clinical practice are clarified and additional information is presented.

Beginning in 1935, the Codman saber-cut approach was used for exposure of the subacromial structures. The practice of holding the acromial fragments by suture of only the soft parts improved the results as to pain and early motion appreciably, and no nonunions occurred.

Since 1938, excision and discard of the outer acromial fragment has been entirely satisfactory. Irregular outgrowths of the bone from the acromial stump, seen in the late roentgenograms, produced no symptoms.

Removal of a calcific deposit from the rotator tendons is done simply through a small, high, deltoid-splitting incision without division of the acromion. Recovery of function was rapid, provided the coracoacromial ligament was divided. Removal of the acromion leaves no functional defect and little or no cosmetic defect, but does not increase the available motion in a stiff shoulder.

In repair following excision of the acromion it is imperative that the deep central tendinous portion of the deltoid origin be firmly incorporated in the suture line. Sutures through muscle substance alone proved inadequate.

The coracoacromial ligament is a major offender in most painful shoulders and routine division of it suggests that the marked reduction in postoperative pain may result largely from release of tension by its division. No glenohumeral instability has resulted. "Snapping" shoulder proved usually to result from (1) thickened bursal walls from a primary irritative focus, which snapped under the edge of the ligament upon arm motion, or (2) irregularity of the bursal floor from a quiescent deposit or small cuff tear so placed as to snap under the ligament with certain motions. Division of the ligament relieved both situations promptly.

Rupture of the long head of the biceps usually occurred secondary to a cuff rupture which exposed the tendon to trauma by the acromion. Relief of the symptoms and disability were dependent on adequate cuff repair, in which the intra-articular portion of the tendon was often split and used as an autogenous suture. No functional defects were observed to result from this procedure.

The frequent observations that avulsions and lacerations of the glenoid labrum were seen in shoulders never dislocated, and that an intact labrum was found often at operations for recurrent dislocation suggested that per se the glenoid labrum was an insignificant factor in recurrent dislocation. Repeated partial excision of the labrum resulted in no functional defects.

The subdeltoid bursa presented several interesting findings contrary to common conceptions. In stiff

TABLE III.—THE FUNCTIONAL RESULTS

Operative repair (100 cases)	Massive avulsions (18 cases)	Complete tears (66 cases)	Incomplete tears (16 cases)
No motion defect	4	44	8
Elevation defect of less than 20 degrees	7	17	6
Elevation defect of more than 20 degrees	7	5	1

shoulders the bursa was smaller and drier than normal, compatible with disuse atrophy rather than so-called "adhesive bursitis." The exceptions were in lesions previously caused by trauma, infection, or prolonged inflammation at the site of calcific deposit. No anomalous communications between the subdeltoid bursa and the shoulder joint were found. All communications resulted from trauma, degeneration or a combination of the two.

Careful study clarified the role of the musculotendinous cuff in elevating the arm. It was proved beyond doubt that some function of the cuff unit was necessary to the elevation of the arm, and that supraspinatus function per se was not necessary for the initiation or maintenance of abduction.

Many widespread diagnostic concepts of cuff tear proved fallacious, only two constant signs of value to the differential diagnosis being established: (1) absence of restriction of passive motion and (2) selective myopathies.

Within 2 weeks from the time of rupture, atrophy was apparent in the spinati bellies, while the deltoid, if changed at all, was hypertrophied. The only two pathognomonic criteria found were (1) arthrographic findings and (2) gross displacement of a fractured tuberosity fragment. Cumulative evidence indicated that in many cases no repair was needed, and in most cases early repair was contraindicated unless massive damage was evident. If after 2 weeks of observation improvement was seen following conservative therapy, this regime was continued. The most efficient conservative treatment consisted of the use of a sling and swathe, which were discarded as soon as the symptoms permitted, palliative measures to control pain, and early resumption of use of the arm at frequent intervals up to the limits of fatigue or pain.

The patients who failed to show improvement on the conservative regimen were operated upon with technique adapted to the individual situation, with only three essential prerequisites:

1. Restoration of continuity between the short rotator muscle bellies and the humerus
2. Snug apposition of the healthy tissues without tension, at the site of repair
3. Restoration of a smooth surface for articulation with the acromion, or removal of the acromion.

Postoperative care might well include a week of complete rest of the shoulder, but this group of patients was managed according to the conservative care which has been previously outlined in this article.

Of interest was the fact that the regular patients returned to work in 50 per cent of the time required by those with compensation. The mobility obtained was rated on the basis of active motion against gravity. It was normal in 56 cases, lacking less than 20 degrees in 30 cases and more than 20 degrees in 13 cases.

Many of the points discussed confirm the previously published postulates of Codman.

FRANCES E. BRENNECKE, M.D.

Dislocation of the Multangulum Majus or Trapezium and Its Treatment in 2 Cases with Extirpation. C. L. PETERSON. *Arch. chir. Neerl.*, 1950, 2: 369.

Complete dislocation of the trapezium is a rare lesion. The first case was reported by Monsengeil in 1871. Eight cases have been reported so far. The author reports 2 cases in this article.

The lesion is classified into 2 types: (1) posterior dislocations and (2) anterior dislocations. The first is the least common type. The displacement is associated with complete loss of relationship with the carpals. The second type is 3 times as common as the first type. The trapezium is dislocated anteriorly as well as in a medial, or lateral, direction. The base of the first metacarpal is displaced in an anteromedioproximal direction.

The chief clinical feature is the appearance of the thumb, which is parallel to the index finger in a position of extension and adduction. Movements of the thumb at the carpometacarpal joint are limited or lost completely. On palpation, there is a definite depression in the normal location of the trapezium. The cause is essentially direct trauma. Roentgen-ray examination reveals the correct diagnosis.

Both of the author's patients were treated by operative extirpation of the trapezium. The hand was not immobilized, and active motion was begun early. Excellent functional and anatomical results were secured in both patients.

DONALD C. GEIST, M.D.

Causal Treatment of Lunatomalacia. Further Experiences with Operative Lengthening of the Ulna. MAURITZ PERSSON. *Acta chir. scand.*, 1950, 100: 531.

Osteomalacia of the lunate bone frequently follows an injury to the wrist, but just as often it develops spontaneously. Hulten suggested that the articulating surface of the distal end of the radius frequently protrudes further distally than the distal end of the ulna. The articulating disc that covers the ulna is soft and resilient and therefore the hard protrusion of the radius injures the lunate bone. This may also explain why osteomalacia occurs more frequently in the lunate bone than in the other carpal bones.

Persson, in 1945, suggested a lengthening osteotomy of the ulna. He suggested that by lengthening the ulna the strain on the lunate bone is diminished. Prior to 1945, 19 patients with osteomalacia of the lunate bone were operated on. In some the radius was shortened; in the others, the ulna was lengthened. Between 1945 and 1949, 14 patients were subjected to lengthening osteotomy of the ulna, but the x-ray films of the wrist did not show material changes within the lunate bone. Since traumatic arthritis in the radiocarpal joint was observed in most of the patients prior to surgery, no definite conclusions can be drawn along these lines.

A detailed description of the operation and roentgenograms of the wrists operated on are presented in the article.

GEORGE I. REISS, M.D.

The Technique of the Claw Hand Operation in a Patient with a Short Stump of Forearm (Zur Technik der Greifarmoperation bei kurzen Unterarmstuempfen). ROBERT SCHISTEK. *Helvet. chir. acta*, 1951, 18: 72.

The usual procedure in constructing a claw hand from the stump of the forearm is to use the ulnar stump as the fixed branch of the grasping mechanism and, as the nonfixed branch, the stump of the radius. The ulnar stump is fixed at any desired degree of flexion or extension of the elbow joint by training the normal antagonists, the brachialis muscle in front and the biceps brachii behind, to act as synergists. The movable branch is opened by contraction of the humeral caput of the pronator teres and biceps brachii muscles, on occasion these muscles being supplemented by the brachioradialis, the extensors carpi radialis longus and brevis muscles. The closing of the prehensile mechanism, that is, the approaching of the stump of the radius to that of the ulna, is effectuated by the ulnar caput of the pronator teres and the supinator muscles.

These arrangements are sufficient in a stump which is 17 cm. in length, and this length of stump is the only one on which such an operation is ordinarily attempted. Shorter stumps are usually merely provided with a prosthesis of some sort. In the case discussed, however, the stump was only 13 cm. in length, but the patient's eyesight was extremely defective and this seemed to render a sensitive grasping arm more than ordinarily desirable.

Under these circumstances the usual operation was altered in the sense that the flexor digitorum profundus muscle was brought over and attached to the stump of the radius to compensate for the loss of the distal attachment of the pronator teres.

Another deviation from the usual technique was dictated by the need for sensorily intact grasping surfaces. A special incision permitted the stump's own cutaneous covering to be folded in around the two branches, leaving only the commissural area of the newly formed grasping mechanism to be covered by skin grafting; this graft was obtained from the skin of the trunk.

This special incision began proximally over the ulna, coursed to the end of the stump of the ulna and then passed across the end of the stump to the stump end of the radius. It then followed back up the stump on the radial side over the mass of the extensor muscles. This incision is illustrated by a series of sketches in Figure 1, and the final result is shown in Figure 2. JOHN W. BRENNAN, M. D.

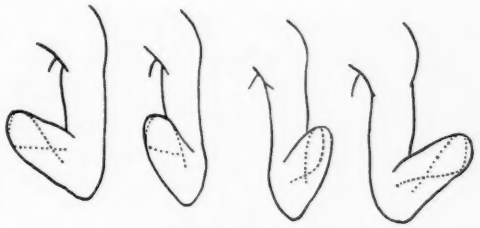

Fig. 1 (Schistek).

Fig. 2. Final result.

The Technique, Indications, and Results of Arthroplasty of the Hip Joint with Interposition of an Inert Substance (Technique, indications et résultats de l'arthroplastie de la hanche avec interposition inerte). R. MERLE D'AUBIGNÉ, J. CAUCHOIX, J. RAMADIER, and M. POSTEL. *Presse méd.*, 1951, 59: 77.

Up to November 1, 1950, 215 arthroplasties were done by the Smith-Petersen method with the vitallium cup, or with the acrylic prosthesis of Judet. Of this number, 151 were selected, comprising those done by the Smith-Petersen technique prior to April 1, 1950, and those done by the method of Judet prior to June 1, 1950. Of the latter, 136 were examined for postoperative revision after an interval of at least 6 months.

Of the 151 selected patients, 2 have died; however, these deaths had no relationship to the operation. For the remaining 149 arthroplasties of this group an arbitrary numerical scale, from 0 to 6, was used to estimate the degree of improvement, or absence thereof, with reference to the three principal manifestations complained of (pain, stiffness, and inability to walk). By assessing these manifestations in this manner the authors are able to report 12 excellent, 9 good, 7 rather good, and 2 mediocre results following the Judet method of treatment for old traumatic fractures of the femoral neck, and 3 excellent, 2 good, 7 rather good, and 4 poor results for the nontraumatic, degenerative arthroses.

With the Smith-Petersen method there were 10 excellent, 10 good, 15 rather good, and 10 poor results for the arthroses. In addition to this last group, there were 27 patients who underwent the Smith-Petersen technique but were supplied with the acrylic prosthesis of Judet, instead of the vitallium cup; in these cases there were 4 excellent, 5 good, 11 rather good, and 7 poor results.

The 13 bilateral cases (26 operations) were less easy to assess, because the generally poor preoperative condition had to be given consideration. In all of these the Smith-Petersen method was used. Three of the patients showed marked amelioration of their previously helpless condition; in 5 the results might be regarded as good, in 1 the results were rather good, and in 4 they were poor, that is, there

was no noticeable improvement following the intervention.

These findings, although the number of cases were too few to admit of definitive evaluation and the time was too short to judge of ultimate improvement, show that arthroplasty by these methods is far from the panacea claimed by certain authors; nevertheless, these methods afford very satisfying results in certain forms of hip disease. In the posttraumatic necroses of the head of the femur, resection and the acrylic prosthesis are indicated with the understanding that the results will be much better if the operation is carried out early, that is, before resorption of the cervical stump and secondary involvement of the acetabulum. In the arthroses secondary to the subluxations or following the dystrophies of the head, the arthroplasty should be done early. In the true arthritides of the hip the arthroplastic operation should be delayed until the condition of the patients can be improved as much as possible. In the cases in which a considerable burden is to be placed on the static processes of the joint itself (standing on feet, prolonged walks) an arthrodesis may be preferable, particularly in those instances in which there is already a considerable loss of joint mobility.

The method of Judet is preferable in the patients in whom the acetabulum is relatively intact and the head is extensively deteriorated. The arthroplasty of Smith-Petersen will be preferred in the case in which the neck of the femur is sufficiently long and with extensive involvement of the acetabulum. The arthroplasty of Smith-Petersen, but with substitution of the acrylic prosthesis of Judet for the vitallium cup, is suitable for the patients with extensive involvement of both the head of the femur and the acetabulum. In the unilateral ankyloses the condition is not tampered with except for vicious postural condition of the ankylosed limb; in bilateral ankyloses the Smith-Petersen technique and the vitallium cup find their indication, this method affording a greater degree of ultimate mobility of the joints than the acrylic prosthesis of Judet.

The old neglected congenital luxation of the hip joint should not be operated upon except in the presence of serious functional troubles; in these instances reduction with arthroplasty and the vitallium cup will afford results superior to the palliative operations thus far utilized.

JOHN W. BRENNAN, M.D.

Results of Surgery in Sciatica, and Low Back Pain. B. H. BURNS and R. H. YOUNG. *Lancet*, Lond., 1951, 260: 245.

Of 913 patients whose discs were inspected at the time of surgery, the authors were able to follow up 717. A protrusion or a lesion of the disc was found in 832 of the patients and of these, 616 with protrusion and 60 with a lesion (degenerative) without a protrusion were followed up.

The results of operation on 616 patients with disc protrusions were as follows:

Group	No. cases	Per cent	
No pain or disability	349	56.6	72.5
Occasional pain	98	15.9	72.5
Improved	125	20.3	
Failures	44	7.2	

Neither the age of the patient nor the duration of the symptoms affects the prognosis; 111 of the patients were 40 to 75 years of age and their results were similar to those in the younger age groups. The results are as good after many attacks as after a few. The large majority of patients with eventual cures are free from pain at the end of 4 weeks, by which time they leave the hospital.

If the patient has another attack after 3 or more months of painlessness it is due to another protrusion, either of the same disc or of a neighboring one.

Eighteen patients with recurrences came to re-exploration, and in each case a further protrusion was found. Re-exploration was not difficult because, as is to be expected in patients with freedom from symptoms between attacks, access was not blocked by adhesions. A protrusion of another disc was commoner than of the same one in the proportion of 2 to 1.

Of the failures, 44 patients had had continuous pain since the first operation, at which a definite protrusion had been removed. Twenty-two of the worst of these were re-explored; in 9 of the 22, another protrusion was found at operation; 6 of these were removed from another disc, one of twins, having been present but overlooked at the first operation. This emphasizes the necessity of inspecting both discs, even when a satisfactory protrusion is found at one.

With dense perineural and peridural adhesions, the root and dura are stuck to the more mobile posterior part of the spinal canal, the back of the foramen, and the lamina. This condition can cause severe sciatica and back pain.

The results obtained in 82 lesions without protrusions (soft spots, bulging discs, and scarred discs) were also analyzed. As might be expected, the results were found to be about half as good.

The discs in 50 patients with low back pain only were inspected at operation. In 30 cases there were protrusions and in 15 cases lesions without protrusions were found. In the presence of a protrusion, the cure rate was similar to that in sciatica. In the presence of a lesion without a protrusion, the prognosis was half as good. Lesions without a protrusion are treated better by fusion. The minimal back signs allow them to be distinguished from the larger protrusions which cause severe pain and severe restriction of forward flexion.

In sciatica, the size of the protrusion varies directly with the restriction of straight-leg raising. Thus, if the patient can raise the straight leg only a few degrees from the bed, the presence of a large protrusion is nearly certain. The rare exception is due to the fact that the protrusion has returned largely as a result of the anesthesia and the position-

ing. It will sometimes reappear on making the patient cough. By contrast, if a patient is operated on in a quiescent period after an attack, when he has no physical signs, a large protrusion will not be found, but only a soft spot or bulge. If a patient with a grossly diminished disc space, as seen in the x-ray film, and a long history of disc trouble (or with long-standing, chronic pain) suffers a new "acute" attack, it is due to a fresh protrusion in another disc; the old disc is extinct, so to speak, and incapable of causing a florid attack of sciatica or back pain. In fact it is often not accompanied by any symptoms at all.

Sciatic scoliosis and the less common scoliosis with back pain only (lumbago scoliosis) are nearly always associated with a protrusion of the disc between L4 and L5. A protrusion of the disc between L5 and the sacrum does not cause well marked scoliosis, although it quite commonly causes a slight sideways tilt or list on forward bending. The direction of the tilt is determined by the position assumed in an attempt to avoid, or to lessen, pressure on the nerve root. Thus, if the protrusion is lateral to the root, the tilt will be away from the side of the pain, because in this attitude the root tends to be removed from pressure; whereas, if the disc is more centrally placed, or in the axilla of the root, the tilt will be towards the painful side (homolateral), because this is then the most relaxed position for the root.

A midline protrusion causes only backache unless it is very large or consists of the greater part of the posterior annulus, when it often causes bilateral sciatica. Pain on hyperextension of the posterior borders of the bodies nip the protrusion, like squeezing a balloon, and make it more prominent. Protrusions of the disc between L3 and L4, or between L2 and L3, naturally give signs of irritation of the femoral nerve and not of the sciatic. The back signs are similar, except that the pain tends to be at a higher level and the femoral stretch sign takes the place of straightleg raising. In some cases the annulus over the protrusion becomes thinned and may occasionally form a flabby sac which, according to the posture, fills or empties with nuclear material in a manner comparable to a hernia. This may be found in a patient who is free from pain on lying flat, but who gets it on standing or bending.

There are three conditions in which spinal fusion is the operation of choice, two well defined, the third condition less definite: (1) spondylolisthesis, (2) adhesions following removal of a disc, and (3) certain cases of backache.

Where there is evidence of a disc protrusion as well, the spine should be explored and the disc removed. The protrusion is usually, but not always, at the same level as the spondylolisthesis. Grafting should always follow removal of the disc; otherwise the slipping may increase. This happened in 2 patients in whom grafting was delayed.

The authors also made use of compression factors by the addition of a spring washer to the bolt, to provide continuous pressure to the grafts against the spinous processes. Although only 14 patients were treated by this method, there has been a remarkable improvement both in the prospect and in the rate of union. Union at 6 weeks has been demonstrated by exploration and confirmed by microscopy. C. Fred Goeringer, M.D.

Leg-Lengthening. F. G. Allan. *Brit. M. J.*, 1951, 2: 218.

This article is based on 101 personal cases. Of this number, 54 patients were subjected to lengthening of the tibia.

In one case with over 6 inches (15 cm.) of shortening, the femur was lengthened twice and the tibia once. In all, about 7 inches (10.5 cm.) of lengthening was obtained, but as the procedure was started when the child was 13 years of age, the normal leg was still growing, and at the end of this period of growth a shortening of 1 inch (2.3 cm.) persisted. There was an interval of about a year between each stage.

In another case, both the femur and tibia were lengthened a total of 4½ inches (11.25 cm.) in a 2 year interval. In a boy with an 8 inch shortening (20 cm.) following tuberculous arthritis of the hip, the legs were equalized by lengthening the short limb 5 inches (12.5 cm.)—2 inches (5 cm.) above and 3 inches (7.5 cm.) below the knee joint, shortening the normal tibia by 2 inches and compensating for the remaining inch by pelvic tilting. The greatest gains in length have been 3½ inches (8.75 cm.) in the femur (1 case) and 4½ inches in the tibia (2 cases). The average lengthening in the whole series is 2½ inches (6.35 cm.) in the tibia and 1¾ inches (4.4. cm.) in the femur.

The indication for leg lengthening is a shortening exceeding 1½ to 2 inches (3.75 to 5 cm.) with a mobile pelvis, or exceeding 1 inch (2.5 cm.) if no compensation is possible by pelvic tilting.

Contraindications are (1) faulty nutrition of the short limb; (2) shortening so great that amputation and the fitting of the prosthesis would be a better plan; (3) active or recently active bone or joint disease; (4) age: only adolescent and young adult patients are suitable; and (5) poor control.

It is sometimes worth while to lengthen a completely flail limb, to be rid of a heavy and unsightly high boot.

There are three possible operative methods of limb equalization: (1) limb lengthening; (2) limb shortening; and (3) arrest of epiphyseal growth.

There remains the choice of shortening or lengthening. When the alternative is offered, lengthening is chosen even after the comparative simplicity of shortening is stressed.

One difficulty has been to maintain muscle integrity. Voluntary movements of the toes and contractions of the quadriceps are encouraged from the start. As muscle tension rises movement becomes harder, and it is not always easy to distinguish between difficulty in extending the toes due to failure of

nerve conduction and that due to the increased tension in the muscles. As soon as distraction is stopped improvement is rapid, and no case has shown any ultimate loss of muscle power. There is a good deal of apparent muscle wasting, but it must be borne in mind that the muscles have been stretched, so that the loss of bulk is not so great as it may seem.

The various complications are enumerated.

C. FRED GOERINGER, M.D.

Principles of the Surgical and Conservative Treatment of Bunions (Grundsaetzliches zur operativen und konservativen Behandlung des Hallux valgus). W. THOMSEN. *Zschr. Urol.*, 1950, 80: 128.

The author believes that the main reason for bunions is shoe pressure. In addition to antagonistic muscle pull, the tension of the plantar fascia is considered an important pathological factor.

Generally, bunion operations are carried out too late, when the basal joint of the big toe is already irreparably damaged. As prophylaxis, manipulation of the big toe in the medial direction is recommended in order to stretch the shrunken lateral capsule. As prophylaxis and also as a postoperative measure, the author describes a splayfoot bandage in which a Quengel windlass device is incorporated; this secures medial displacement of the big toe.

E. H. BETTMANN, M.D.

Experiences with Bunnell's Pull-Out Wire Sutures. ERIK MOBERG. *Brit. J. Plast. Surg.*, 1951, 3: 249.

The writer made use of the pull-out wire suture in 101 cases of hand surgery. In most of the cases the suture was completely satisfactory.

The results of free tendon transplantation have been superior to both those of primary and secondary tendon suture despite the longer time for treatment necessary with this method.

Remarkably good results were obtained not only when the technique was used for suturing tendons but when it was used for suturing ligaments to the skeleton. The technique was used also for suturing the attachment of the ruptured dorsal aponeurosis to the base of the middle phalanx in 9 cases and to the base of the distal phalanx in 16 cases.

The author cautioned against attaching the tendon graft too far distally on the phalanx in instances of flexor tendon attachment because the flexor may be made so much stronger than the extensor that a flexion contracture might develop. In 2 cases this result was so marked that the patient could not easily release his grip, and the joint was later arthrodesed in slight flexion.

When the tendon has been fixed to the distal phalanx, the suture wire is tied to the free border of the nail after a hole is made in it. The wire is pulled out after 3 to 5 weeks. In no case was the postoperative course of the patient disturbed by infection, nor was there any later loosening of the fixation of the tendons or ligaments.

C. FRED GOERINGER, M.D.

FRACTURES AND DISLOCATIONS

Fractura Capituli et Trochleae Humeri, a Rare Elbow Fracture. W. A. MOONEN. *Arch. chir. Neerl.*, 1950, 2: 385.

The author discusses fracture of the capitellum and trochlea of the humerus. Four patients with this condition were seen in the author's clinic; all of them were women. Three of them were seen some time after their injury, but 1 was seen immediately after the fracture had occurred. Only the last patient was treated by surgical extirpation, with an excellent result.

This injury, first described by Hahn in 1853, is a rare one. It consists of a breaking-off of the condylar surfaces of the capitellum and trochlea. The fracture surface runs parallel to the anterior humeral surface and only the pars anterior is broken off. The bone segment is displaced upward and forward and rotates 90 degrees on its horizontal axis.

There is a difference of opinion as to the causative mechanism. Some believe a fall on the hyperextended elbow causes the injury. Hyperextension and valgus flexibility of the elbow were present in all of the author's patients. A constitutional factor cannot be excluded.

Surgical extirpation should be done promptly after injury. Technical points are discussed. Functional restoration is attained soon after removal of the bone fragment, and the result is good.

DONALD C. GEIST, M.D.

Residual Subluxation of the Hip After Reduction for Congenital Dislocation (Subluxaciones residuales de la cadera consecutivas al tratamiento de las luxaciones congenitas). PIERRE BERTRAND and LUIS J. PETRACCHI. *Rev. orthop. traumat.*, B. Air., 1950, 20: 120.

The authors designate residual subluxation as a condition in which, after reduction for congenital dislocation of the hip, the head of the femur is imperfectly placed in the acetabulum.

The main etiologic factors are imperfect reduction of the dislocation, epiphysitis, and vicious orientation of the neck of the femur. These conditions could be recognized early and the consequences avoided with systematic use of arthrography. In some cases the residual subluxation presents itself after surgical reduction. This happens especially in cases in which the surgical intervention is performed before the child has reached the age of 2½ years.

The pathologic findings are as follows: the head of the femur is enlarged and flat, and the acetabulum is shallow, or even convex, instead of being concave. The clinical symptoms, in the beginning, are usually very vague and consist mainly of fatigue, with a limp in the afternoon. If the condition is not treated in time, the result is a deforming arthritis in adulthood; therefore it is very important that treatment be administered as soon as the diagnosis of subluxation is made. In cases in which the disease is not advanced the orthopedic method of treatment

is preferred. The authors recommend the application of a cast in abduction and inward rotation. In the more advanced cases, surgical reduction is necessary. In the authors' cases, the best results were obtained with extraarticular rotation osteotomy. Nevertheless, they believe that in future the treatment of choice will be intraarticular arthroplasty.

OLGA M. HARING, M. D.

The Luxations of the Patella with Exclusion of Recent Traumatic Luxations (Les luxations de la rotule en dehors des luxations traumatiques récentes). JOSEPH MARION and JEAN BARCAT. *Rev. orthop.*, Par., 1950, 36: 181.

This study is based on 273 cases of luxation of the patella taken from the literature and principally on the clinical investigation of 218 cases observed by colleagues at home and abroad, making a total of 491 cases, of which 213 offer late results after more than 3 years.

Spontaneous luxations of the patella are distinguished from true traumatic luxations by the presence of previous anatomic lesions, which are of congenital, traumatic, or pathologic origin. The various clinical forms correspond to different lesions and mechanisms; therefore, the operative intervention must provide each lesion with its best correction. However, certain rules must guide the choice of the intervention and the conduct of the treatment.

1. The necessary operation must be performed immediately.

2. The choice of the intervention must be preceded by a careful etiologic and anatomoclinical examination, various positions being used in taking the axial films and the serous pneumograms.

3. The choice of incision is important: flap incisions are condemned because they often lead to necrosis, but straight or curved incisions of adequate length often suffice. The incision of Dupuis can be used for practically all current techniques.

4. The operation must be performed gently with excellent hemostasis.

5. Postoperative care is highly important; with strong fixation and sutures, the cast may be removed rapidly or even omitted, active contractions of the quadriceps may be started 4 to 5 days after operation, mobilization on the tenth to twelfth day, and walking with caution after 2 or 3 weeks.

Recurrences are numerous, from 15 to 20 per cent; they may be early or late, generally during the first 3 years. In addition to complete recurrences, there are residual, slight, or infrequent recurrences, and internal subluxations due to excessive correction.

The results are much worse in the congenital luxations, especially in their permanent and habitual forms; they are excellent in the traumatic luxations. The high percentage of recurrences observed in children operated upon before the age of 10 represents probably an aspect of the influence of congenital malformations. The frequency of pre-existing signs of arthrosis explains the higher proportion of bad results in adults.

All operations on the soft parts invite recurrences. Even Krogius' method often fails, and it is frankly bad for the permanent or habitual forms of congenital luxations. Its results are better in the recurrent forms and very good in the traumatic luxations, at least when the true Krogius method is used, which seems to be decidedly superior to the modified Krogius-Lecène technique.

Osteotomy alone is nearly always insufficient. Albee's method has been used only as a complement and its efficacy is difficult to demonstrate; however, it does not seem to present the articular drawbacks that have been attributed to it. There is insufficient information about patellectomy, but it does not protect absolutely against recurrence.

The mixed operations (Roux, Mouchet, Fèvre-Dupuis) seem to be the best. Goldthwait's procedure seems to favor recurrences. Extrasynovial operations ensure more rapid and better recuperation.

RICHARD KEMEL, M.D.

ORTHOPEDICS IN GENERAL

Late Results in Legg-Perthes Disease. EUGENE R. MINDELL and MARY S. SHERMAN. *J. Bone Surg.*, 1951, 33-A: 1.

The present study was undertaken in an attempt to evaluate the treatment of Legg-Perthes disease in terms of the end results.

Seventy-two patients with 78 involved hips form the basis for this study. Half of them were followed up for from 6 to 15 years and 6 were followed up for more than 25 years. In two-thirds of the cases, growth from the upper end of the femur has been completed.

The type of therapy is classified as ambulatory or nonambulatory. Ambulatory treatment refers to the use of crutches without weight bearing, or, in some cases, to an ischial weight-bearing brace. Nonambulatory treatment includes prolonged periods of bed rest, traction, or immobilization. The length of treatment in these two groups was essentially the same.

It is evident that the patients who were treated early have a much higher incidence of good results than those who were treated late or not at all. No significant difference can be demonstrated in the results following the use of ambulatory or nonambulatory methods of treatment. Both methods produced a high percentage of good results.

The fact that younger patients have better results has several possible explanations. The femoral capital ossification center is smaller and is protected by a relatively thicker layer of cartilage and, in addition, less weight is placed on the necrotic femoral head by a smaller child. Younger children also have a longer active growing period during which the upper portion of the femur may be remodeled.

It was possible to follow abnormalities of the femoral neck in 53 cases. The usual change consisted of a diffuse, irregular zone of decreased density in the metaphysis. Occasionally, successive lesions

developed in the subepiphyseal area and each followed the same pattern. Eight patients, or 15 per cent of this group, had large discrete lesions, often surrounded by thin sclerotic walls and sometimes associated with collapse of the overlying femoral head. Of these 8 patients, 6 had poor final results, 1 a fair result, and 1 a satisfactory result. It seems, therefore, that extensive changes in the femoral neck generally indicate a poor prognosis.

The prognosis in a case of Legg-Perthes disease can in a general way be estimated early in its course. Younger patients have been shown to have a higher incidence of satisfactory results. Evidence of severe disturbance of the femoral neck with damage to the epiphyseal plate is followed by deformity and a poor result. Often only a portion of the epiphyseal cartilage is damaged and the result is asymmetrical growth retardation, which may not become evident for some time.

Marked changes in the femoral neck, and lateral expansion or central depression of the femoral head indicate a bad prognosis. In general, the younger the patient at the onset of the disease, the better the prognosis. Premature symmetrical or asymmetrical growth arrest of the capital femoral epiphyseal cartilage plate may occur in some cases and contribute to the deformity.

C. Fred Goeringer, M.D.

Reconstruction of the Thumb (Reconstruction du pouce). R. Merle d'Aubigné, R. Tubiana, and Ramadier. *Mém. Acad. chir.*, Par., 1950, 76: 901.

Eight interventions for reconstruction of the thumb are reported. In 3 of these 8 instances, in addition to the mutilation of the thumb, there were more or less important lesions of the index finger. In these patients the injured index finger was utilized for rebuilding the thumb. In 1 of these patients, the metacarpal of the thumb was also lost and the pollicisation of the entire remnant of the index finger, together with the corresponding metacarpal bone, resulted in too long a thumb. The author thinks that, on the whole, the substitute thumb should be just long enough to be reachable by the tips of the remaining fingers.

In the 5 cases in which the fingers, other than the thumb, were not injured, autoplasty was attempted. At first the skin of the abdominal wall, reinforced by a bone transplant from the iliac crest was used. Later, the skin covering the bone of the substitute thumb was procured from the neighboring tissues of the hand itself in order to have a new thumb with as little loss of sensitivity as possible. In one instance an extensive arciform incision was passed around the base of the first metacarpal; as massive an internal pedicle as practicable was left in order to conserve as much as possible of the blood and nerve supply passing through the tissues between the thumb and first finger; the resultant raw area was later covered by a free skin graft.

In general, it is desirable to seek mobility of the metacarpal bone. In the event that this is not possible, the substitute for the metacarpal or the poorly mobile metacarpal itself had better be solidly implanted on the abutting carpal bone. The matter of apposition with the remaining fingers should be carefully attended to. In the transferences of the index finger as a substitute (pollicisation), the mobilized finger should be rotated through at least a 90 degree angle and should be firmly secured in this position until healing is complete. Of course, the blood vascular and nerve supplies should be spared as far as possible. It is important to have in the new thumb not only strength, but also sensation; the hand thus reconstructed should be able to grasp not only bulky and more or less weighty objects but should be capable of grasping and retaining such tiny objects as the ordinary pin or needle.

In the discussion, Oudard describes a case in which he transplanted the 2 distal phalanges of the big finger, of the opposite hand to form the new thumb. In this case he claims to have procured a thumb which, in spite of some apical atrophy of the implant, had an absolutely normal sensitivity and even felt cold in winter. The author, however, disapproves of all such methods because they are too complicated and prefers his described methods as they are simpler and sufficiently efficacious in most instances to permit ordinary use of the hand.

John W. Brennan, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Congenital Vascular Anomalies. Acors W. Thompson and June C. Shafer. *J. Am. M. Ass.*, 1951, 145: 869.

In an attempt to simplify the nomenclature concerned with congenital vascular anomalies of the extremities, the authors present a brief review of the terminology, pathogenesis, and clinical description of these unusual and complex lesions. These malformations, arising from mesodermal dysplasias, may demonstrate many variants due to the stage in their embryologic development at which the maturation process is arrested. An abnormal development of arteries and veins from the vascular primordium or capillary plexus would seem to afford the chief explanation of the occurrence of vascular anomalies. The retention of embryonal characteristics by vascular segments may also explain the formation of the angiomas.

In the majority of patients, angiomatous lesions are apparent at birth or shortly thereafter, and trauma, while often considered the cause, is actually only a precipitating agent. Congenital arteriovenous fistulas present a variable picture depending on their size, location, and number. In an extremity there may be dilatation of the veins, a pulsating vascular mass, elevation of the skin temperatures, hypertrichiasis and hyperhidrosis, and enlargement of the extremity if the fistula is functioning before the epiphyseal centers fuse. Cutaneous atrophy and ulceration may be seen as late effects. Venous oxygen saturation studies may identify the presence of an arteriovenous fistula and arteriograms are also helpful.

Phlebectasia, apart from varicose veins, is a venous malformation presenting gradually developing multiple, spongy, bluish, irregular venous sinusoids often first appearing clinically during childhood. They may be 1 to 5 cm. in diameter, although wide variations in size are seen. This condition is to be differentiated from the tortuously dilated but normal anatomic pattern of the varicose vein complex, but oxygen saturation studies may be required to rule out arteriovenous fistula.

Iodopyracet is recommended for injection and three common characteristics of arteriovenous fistulas are mentioned: (1) dilatation of the arteries leading to the fistula, (2) absence of normal arteries distal to the fistula, and (3) pooling of the medium in the region of the fistula. Congenital anomalies involving venous segments also present three common characteristics: large sinusoid collections of radiopaque substance, (2) irregularity in the caliber of the veins, and (3) clusters of minute collections of radiopaque material scattered irregularly throughout the involved area. An increase in oxygen saturation of the venous blood is indicative of a fistula. Skin temperatures are elevated over arteriovenous lesions, and venous pressures are elevated in the segments adjacent to a fistula, while phlebectasia shows no such alterations.

The following groupings are suggested by the authors: (1) anomalies of large vessels conducting blood to the part (arterial aneurysms), (2) anomalies of large vessels conducting blood away from the part (phlebectasias), (3) anomalies of minute vessels (nevi flammei), (4) abnormal communications between arteries and veins (arteriovenous fistulas), and (5) anomalies associated with combinations of these functional elements. Case reports of 10 patients are included.

Allan D. Callow, M.D.

Twelve Cases of Cirsoid Aneurysm (A propos de 12 cas d'anévrysme cirsoïde). R. Leriche. *Lyon. chir.*, 1951, 46: 5.

Cirsoid aneurysm should be distinguished from congenital arteriovenous fistula and from diffuse capillary angiomatosis.

Of 12 aneurysms operated upon by the author, 8 were located on hands, and 4 were either in the frontal region of the head or on the scalp.

Only the presence of a chill, and a dilatation and elongation of blood vessels in the same area justify the diagnosis of a cirsoid aneurysm. Contrary to popular opinion, the author believes that only a single arteriovenous communication exists in a cirsoid aneurysm. In contradistinction to congenital or acquired fistulas, cirsoid aneurysm produces diffuse hyperemia of the entire involved region, and after even a small incision active bleeding from innumerable intradermal arterialized vessels may be observed. This must occur as the result of sympathetic activity.

Cirsoid aneurysm does not necessarily develop from a pre-existing angioma; it may be the sequel of a trauma in an exposed region. While angiomas show no predilection for any part of the body, cirsoid aneurysms are located in the frontal region of the head, on the scalp, or on the hands.

Active regional vasodilatation plays an important rôle in the pathologic physiology of cirsoid aneurysm. The skin of the involved area is hot. After incision, bright red blood escapes from numerous small intradermal blood vessels. The vasodilatation is secondary to the single arteriovenous communication.

Diffuse rarefaction of the phalanx in the affected area and interference with the growth of the bone may form the first sign of a cirsoid aneurysm.

Three stages of clinical evolution of the lesion may be distinguished: (1) a silent stage during which slight discomfort or a minute pulsating tumor may appear, (2) the stage of growth, when cirsoid features make their appearance and the tumor increases in size, and (3) stage of hemorrhages and trophic disturbances, such as ulcers.

The short circuit is responsible for the fact that arteriography furnishes confusing results. As to the treatment, resection of a segment of dilated arteries or veins is absolutely useless. The arteriovenous communication must be interrupted. The location of the greatest intensity of the thrill and of trophic disturbances furnish clues to the site of the communication. JOSEPH K. NARAT, M.D.

Treatment of Arterial Occlusions. Comparative Value of Thrombectomy, Thromboendarteriectomy, Arteriovenous Shunt, and Vascular Grafts—Fresh Venous Autografts (Sur le traitement des oblitérations artérielles. De la valeur respective des thrombectomies et thrombendartériectomies, des shunts artério-veineux, et des greffes vasculaires—autogreffes veineuses fraîches). R. FONTAINE, P. BUCK, R. RIVEAUX, M. KIM, and J. HUBINONT. *Lyon. chir.*, 1951, 46: 73.

The clinical evolution of arterial occlusion may be divided into four stages: (1) the latent period; (2) ischemia after effort, manifesting itself in the form of intermittent claudication; (3) ischemia at rest; (4) complications such as ulcers and gangrene. The success of sympathectomy is greatest in the second, and, to a lesser degree, in the third stage of arterial occlusion. In recent years sympathectomy has been supplemented by a number of procedures whose aim is to re-establish the permeability of occluded arteries. One such operation is thrombectomy. If the thrombus is extensive and adheres to the wall of the artery, so-called thromboendarteriectomy may be necessary. In this operation the thrombus is excised together with the adjoining part of the intima. Inasmuch as the effect is due not only to mechanical factors but also to vasodilatation of sympathetic origin, the procedure may properly be termed "intramural neuroendarteriectomy." The second type of operation is represented by arteriovenous shunts, and the third type by venous or arterial grafts, either fresh or preserved.

The authors review the results of surgical procedures employed in 64 patients with arterial occlusions. Thrombectomy or thromboendarteriectomy was employed in 27 cases, arteriovenous shunts in 9, and fresh venous autografts in 28 cases. Of the first group of 27 patients, the involved artery remained patent after the first year in only 3. Of the 9 patients in whom arteriovenous shunts were employed, only 2 benefited from the shunt. Arteriographic studies showed that after the use of venous autografts the involved artery remained patent in all 6 patients with posttraumatic occlusions. Of 22 patients with occlusions of nontraumatic origin, 10 had patent arteries for 1 to 10 months after grafting, while in the remaining 12 cases secondary thrombi developed; however, the clinical result even in these cases was excellent.

The authors intend to employ preserved arterial grafts for reconstruction of occluded arteries. From their observations, they concluded that grafts furnish superior results to those of other surgical procedures. JOSEPH K. NARAT, M.D.

Experimental Findings and Theoretical Considerations Concerning Superficial Varicosities of the Lower Extremities (Données expérimentales et théoriques concernant les varices superficielles du membre inférieur). RENÉ VAN HOVE. *Acta chir. belg.*, 1950, 49: 889.

Manometric records of venous pressure in the lower legs show that it is not influenced by the presence or absence of functioning valves in venous segments above the involved area. The records were made on patients in a sitting position, with the legs hanging. The findings suggest that classical interventions for varices are theoretically of little value.

The author recorded venous pressure in sitting patients who were instructed to contract and relax their triceps and quadriceps muscles. The records were made with and without compression of the internal saphenous vein in the groin. The rapidity and extent of the rise of venous pressure following muscular contractions were more or less parallel in both instances. The fall of venous pressure after relaxation of muscles was more rapid and more pronounced if the perforating branches possessed valves and the latter were of normal size.

The customary operations for varicosities have no effect on the venous pressure in the dilated veins in the standing position, but ameliorate the condition when the patient walks.

The larger the diameter of the vessel, the easier it is subject to abnormal dilatation.

Tangential force which tends to elongate the wall of the vein is in direct proportion to the viscosity of the blood and to the amount of blood passing the involved segment. As a rule, varices of small and medium size are more apt to become tortuous than larger varicosities.

Theoretical considerations indicate that ideal therapy of varicose veins should aim to (1) correct the insufficiency of elastic tissues of the walls of the vein, (2) eliminate the slightest dilatation of the vein before a vicious circle is established, (3) eliminate the largest possible number of dilated segments, (4) avoid reflux of the blood through veins smaller than those resected, (5) diminish the viscosity of the blood, and (6) reduce the volume of the blood passing the dilated portions of the venous system.

The author is aware of the fact that such ideal treatment can not be easily accomplished.

JOSEPH K. NARAT, M. D.

Ambulatory Venous Pressure Determinations in Postphlebitic and Related Syndromes. PAUL T. DECAMP, ROBERT J. SCHRAMEL, CHARLES JOHN RAY, N. DONALD FEIBLEMAN, JAMES A. WARD, and ALTON OCHSNER. *Surgery*, 1951, 29: 44.

Because of the many etiologic factors in the postphlebitic syndromes, a study of the ambulatory venous pressure was made in an attempt to evaluate some of them. Immediately following ligation or thrombosis in a peripheral vein the pressure rises distal to the obstruction. Part of this rise may be

due to reflex vasospasm, which may be eliminated by sympathetic block.

In a normal person the venous pressure drops in the lower leg with exercise, probably because of the pumping action of the muscles in the fascial compartment. Competent valves are thought to aid this action by preventing the reflux of blood. In patients with a postphlebitic syndrome the venous pressure does not fall as much with ambulation as in normal individuals. Since adequate pressure determinations have not been made to prove these theories, the following study was undertaken. Subcutaneous veins of the ankle were used, but it is believed that in this location they represent the end veins of the deep, as well as of the superficial, venous system.

Forty-seven patients were studied. Eight of these were subjected to retrograde phlebography to correlate the anatomic with the physiological findings. In all of them the recumbent antecubital vein pressure was recorded initially at atrial level.

Eleven normal persons were studied to obtain the normal pressures.

Fifteen patients with a postphlebitic syndrome were studied. All but 1 had had ulceration at one time, and all gave a history of edema. Mild superficial varicosities were noted in 12. The mean recumbent antecubital venous pressure was 11.5 cm. The mean recumbent foot pressure was 18.8 cm., and the mean resting erect pressure was 7.3 cm. All of these were within normal range and showed that static venous pressure studies are not good indices compared with ambulatory studies.

On ambulation, the pressure began to drop quickly, requiring 9 to 23 seconds and a mean of 14 seconds. The degree of fall was small so that the mean rate of fall was 2.8 per cent per second as compared with a mean rate of 5.1 per cent per second in normal individuals. The degree of fall ranged from 16.6 to 52.5 per cent, with a mean of 38.0 per cent. Once established during exercise, these rates remained constant. After walking, the rise was rapid, from 3 to 14 seconds, with a mean of 8.8 seconds. The mean rate of rise was 4.4 per cent per second compared with the normal of 2.1 per cent per second. The tourniquet made no significant difference.

Retrograde phlebography confirmed the absence of competent valves in the deep venous system.

Four women with ligation of the inferior vena cava for septic pelvic thrombophlebitis were studied from 1 week to 39 months after operation. All of the patients had minimal edema as the only clinical finding. The mean recumbent foot pressure was 35.1 cm., and the erect resting pressure mean was 17.4 cm., both of these pressures being higher than normal. All 4 of these cases are discussed in detail. Three of the patients showed an initial drop in pressure followed shortly by a sharp rise which remained until the cessation of walking. In 1 the pressure rose directly without an initial drop. All the pressures shot high again at the end of the exercise and slowly returned to resting erect levels.

Four cases of the postphlebitic syndrome that showed the severe obstructive type of curves are discussed in detail. These curves were similar to those of the 4 patients with caval ligation. One of them was made worse by the tourniquet, which suggested that the superficial veins were helping to overcome the obstruction.

Three patients with the postphlebitic syndrome of typical pattern were subjected to vein ligation (in 2 the superficial femoral vein and in 1 the popliteal). After operation all of the cases showed the pattern of increased obstruction. This indicated that venous ligation did more harm than good, although in none of these cases was there any change in the clinical picture.

Nine additional patients who had had ligation previously were studied. All had recumbent and resting erect pressures within normal limits. These showed a lowered rate and a lower degree of fall similar to that in the postphlebitic series. Four of these patients showed a postambulation rise and all of them showed a rapid pressure rise on cessation of exercise.

These studies apparently indicate the fallacy of deep vein ligation in the postphlebitic syndrome.

CURTIS ARTZ, M.D.

Venous Thrombosis; Analysis of 580 Cases. ALTON OCHSNER, MICHAEL E. DEBAKEY, and PAUL T. DECAMP. *Surgery*, 1951, 29: 24.

Venous thrombosis is classified into 2 types: (1) that associated with, dependent upon, and secondary to an inflammatory process of the wall of the vein (thrombophlebitis); and (2) that in which a thrombus occurs without antecedent change within the wall of the vein (phlebothrombosis). The second form is dangerous because lack of inflammation fails to make the clot adherent to the vessel wall and thus it may break free at any moment.

This study is based on an analysis of 580 cases at the New Orleans Charity Hospital. There were 203 cases of fatal embolism, 150 of which were confirmed at autopsy; in 45 of these the condition followed operation.

Two-thirds of the patients at this hospital are colored, but thrombosis was found to be more common in whites than in the colored and more frequent in females than in males. Embolism was more common in males.

The age incidence of fatal embolism follows the curve for age distribution of thrombosis. Fatalities appear to occur at a slightly earlier age from thromboembolism than general hospital fatalities. The seasonal incidence was about the same.

The incidence of thromboembolism for the various services followed the curve of admissions except for gynecology and obstetrics. In these services postpartum obstetric cases with the disease were usually placed on the gynecology service. As a result the incidence of thromboembolism was increased to 18.1 per cent as compared with 9.8 per cent of hospital admissions.

Slightly more than one-fourth of the cases of thromboembolism were on the medical service, and nearly one-half of the fatal cases were on this service probably because of the great number of cardiac patients. Ten per cent of the cases appeared on the obstetric service but only 2 per cent of these were fatal. Surgery included 37 per cent of the cases but only 25 per cent of the fatalities.

The deaths from pulmonary embolism in general followed the curve of hospital deaths except on the obstetric, gynecologic, and tuberculosis services. Gynecology included 1.9 per cent of the hospital deaths but 13.8 per cent of the deaths from embolism. Conversely the tuberculosis service included 11.5 per cent of the deaths but only 0.5 per cent of the deaths from embolism.

An attempt was made to study the cases of fatal embolism by groups to see if any would have been preventable. There were 83 fatalities in cardiac patients, and in only 3 did the emboli arise from leg veins; however, all of the patients had sufficient cardiac disturbance to account for death so that it was unlikely that any could have been saved. Among the postoperative group of 68 cases there were 45 deaths, of which 23 might have been prevented by venous ligation since the patients had definite symptoms in the leg veins prior to death. Among the 106 cases of noncardiac medical, nonoperative thromboembolism there were 75 deaths. Forty-five of these patients had definite signs of venous disturbance in the legs and probably would have been saved by ligation.

Of the total number of patients who died, 50 per cent showed no evidence of thrombosis prior to embolism. The incidence of thromboembolism continues to increase, having risen 56 per cent in the past 10 years. Part of this rise may be due to increased awareness of the condition.

The necessity of a test to indicate impending thrombosis so that anticoagulants can be started to prevent thromboembolism is emphasized. The prothrombin time has been shown to be inadequate. The determination of antithrombin may prove of value. When antithrombin blood levels fell below 1:16, thrombosis began to be evident. Of 30 patients with antithrombin levels below this range, 16 developed thrombosis and embolism. This suggests that the ratio between the prothrombin and the antithrombin is the important point, which would explain why some patients with prothrombin levels lowered by anticoagulants still form thrombi. As the authors believe that alpha tocopherol is a normal antithrombin which is found in the blood, they suggest that this be used in the treatment of patients with a low anti-thrombin titer.

CURTIS ARTZ, M.D.

SURGICAL TECHNIQUE

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

The Management of Burns. R. H. CRAM. *Lancet*, Lond., 1951, 260: 263.

A method of management of burns is presented which emphasizes several important aspects which have been presented before. In the first aid treatment of burns it is recommended that no treatment of the burned areas be done. However, the treatment of shock with a plasma is suggested, as is sedation with general supportive measures such as maintaining only enough heat to keep the patient comfortable until definitive care is started.

The treatment in the hospital is then started by maintaining control of shock. It is permissible to remove the clothing and dress the burns under aseptic conditions. Sedation or anesthesia, depending upon the co-operation of the patient, may be necessary. Foreign bodies such as clothes, ashes, and loose blistered bits of skin are thoroughly and gently washed away. The author advises no scrubbing that may injure the thin remaining epithelium and convert a second degree burn to a third degree burn. After cleansing the burn, a penicillin emulsion or similar preparation is smeared over the area and is covered with a single layer of wide mesh soft paraffin gauze. This is reinforced and firmly bandaged with sterile gauze and preferably elastic bandages. Joints are immobilized in the position of function with plaster splints. This is important particularly in the burns involving the hand in which the fingers are dressed separately and apart. Elevation of the extremity is important in the after-treatment of any burn in the extremities.

The immediate excision of third-degree burns has not been necessary in the author's opinion. A second dressing of the burn is done in from 7 to 10 days under the same conditions and with similar aseptic precautions as in the first dressing; split-skin grafts are applied at this stage if the areas of third-degree burn are well defined. Weekly dressings are then done in the operating theater until the burn is completely epithelized.

The treatment of shock is considered by the author with 2 case illustrations of the methods used in the management of shock of various degrees. The requirements of plasma in each case were different in spite of the fact that the degree of body surface burn was almost equal in both cases. The author suggests that a base-line estimation of the hemoglobin and hematocrit levels be done before hemoconcentration has occurred. These estimations are done at 2-hour intervals until the blood volume is increasing rather than decreasing. When the blood pressure and pulse rate are within normal limits, the primary dressing (in the operating theater) is done. It is advisable to continue the plasma drip for at least 72 hours because of the loss of plasma during this period. Later the hematocrit and hemoglobin estimates are reduced to 6-hour intervals on the second day. The latent anemia which occurs and is noted after the restoration of the blood volume, is corrected by whole blood given after the plasma infusion.

While one is using reconstituted dried plasma instead of normal plasma, it is important to add sodium chloride to the plasma in order to maintain normal blood chloride levels. The urine is usually tested for chlorides in extensive burns, especially in the unco-operative or unconscious patient who is unable to take sufficient salt by mouth to compensate for its loss. The secretion of urine is kept up to 1,500 ml. each day with fluids given by mouth. It is suggested that not all plasma be reconstituted with saline solution because of the danger of retention of sodium when the fluid intake is low. It is advisable that alternate plasma bottles be reconstituted with saline solution. JOHN E. KARABIN, M.D.

The Prophylaxis of Tetanus with Penicillin-Procaine. WELTON I. TAYLOR and MILAN NOVAK *Ann. Surg.*, 1951, 133: 44.

Clinical tetanus is a serious disease with a high mortality. Until recently antitoxin was considered the drug of choice to combat the disorder. It is well known, however, that tetanus antitoxin is of value only in neutralizing the toxin liberated into the tissues by the active growing bacteria. It has no significant adverse effect on the tetanus bacilli, which are destroyed by tissue phagocytes. The prophyiaxis of tetanus by means of the local administration of penicillin was found to be even more effective than prophylaxis with antitoxin alone. Reduction of the mortality from 100 per cent to as low as 5 per cent was observed in many of the animal experiments. The inability of antitoxin to cope with a maximal infection indicates the practical value of penicillin as a prophylactic agent in tetanus, either to supplement the prophylactic dose of antitoxin or to be used in its stead in cases in which it is desirable to prevent sensitization to horse serum.

The results bear out the wisdom of removing the source of toxin with penicillin rather than of depending entirely on antitoxin to neutralize the toxin without an attempt to stop its further production. The use of penicillin-procaine dosages which will maintain a therapeutic level for several days is recommended. STEPHEN A. ZIEMAN, M.D.

Chloramphenicol (Chloromycetin) and Aureomycin in Surgical Infections. WILLIAM A. ALTEMEIER and WILLIAM R. CULBERTSON. *J. Am. M. Ass.*, 1951, 145: 449.

This communication is an appraisal of the clinical effects of two of the newer antibiotics, based on ex-

perience with their use in 233 patients with a variety of surgical infections which were treated in the Cincinnati General Hospital. In all of the cases treated the etiological agents were determined and their susceptibility to penicillin, chloramphenicol, and aureomycin was measured both at the start of treatment and at intervals of 3 to 10 days during therapy. Administration of these drugs was, in most cases, by the oral route, from 25 to 75 mgm. per kilogram of body weight being given in divided doses every 24 hours. When they were given in this way effective antibacterial blood levels were reached within 30 minutes, with peak concentrations occurring within 1 to 2 hours.

In vitro investigation of the various strains of bacteria isolated in these cases showed a wide variation of invulnerability in each species. This was true especially of the Proteus group in which the susceptibility of different strains varied from 0 to 35 per cent for aureomycin and from 25 to 100 per cent for chloramphenicol. Varying percentages of all groups of bacteria commonly associated with surgical lesions were resistant to each of the three antibiotics. Development of resistance under therapy in susceptible strains occurred in 6.6 per cent of the patients being treated with chloramphenicol and in 9.9 and 14.6 per cent of those being treated with aureomycin and penicillin, respectively.

Of 179 patients treated with chloramphenicol, 6 had mild gastrointestinal irritation with nausea and vomiting, 3 had a maculopapular cutaneous rash, and 2 had stomatitis. Side effects occurred in no less than 24 per cent of those treated with aureomycin, and consisted almost entirely of the symptoms of mild or moderate irritation of the gastrointestinal tract.

In a group of 37 patients in whom the infecting organism was the hemolytic Staphylococcus aureus, the response to either chloramphenicol or aureomycin was excellent although the organisms in no less than 11 of these patients were resistant to penicillin in vitro. Only one strain of this infecting Staphylococcus was resistant to chloramphenicol and only 2 strains were resistant to aureomycin. Cure was established in 2 of 3 cases of anaerobic streptococcal infection which had been resistant to penicillin.

The results of treatment in a group of "pure" gram-negative bacterial infections were encouraging, the cases including peritonitis, postoperative wound infections, septicemia, cholangitis, and acute urinary infections. Included was a patient with pylephlebitis, peritonitis and septicemia due to the Escherichia coli, who made complete recovery.

Provided that necessary surgery was carried out concomittantly, the results of treatment in acute mixed infections were excellent or good in from 60 to 70 per cent of cases. Both chloramphenicol and aureomycin seemed to be of undoubted value in the treatment of acute spreading peritonitis or as an aid in surgical incision when an intra-abdominal abscess developed. There seemed to be some merit in giving penicillin simultaneously in such cases.

There is experimental evidence that chloramphenicol and aureomycin possess marked antibacterial activity in vivo for highly virulent and susceptible strains of the Clostridium perfringens isolated from war wounds.

In general, aureomycin is of little value in treating infections due to the Pseudomonas aeruginosa and the Proteus vulgaris. Penicillin is preferable to aureomycin and chloramphenicol in the treatment of gram-positive coccal infections when they are sensitive, but the latter antibiotics should be preferred to streptomycin in gram-negative bacillary infections. The continued necessity for timely surgery is emphasized. It is equally important in choosing antibiotics to establish the nature of the infecting organism and its susceptibility in vitro.

M. R. EWING, M.D.

ANESTHESIA

The Effect of Inhalational Anesthetic Agents on the Myocardium of the Dog. CARL W. FISHER, LESLIE L. BENNETT, and AKHTAR ALLAHWALA. *Anesthesiology*, 1951, 12: 19.

Heart and lung preparations of the dog were made to eliminate the reflex control of the heart rate and thus control it so that neither the venous return nor the peripheral resistance could vary during the course of an experimental observation. Studies were made of the effects of chloroform, ether, cyclopropane, divinyl ether, and nitrous oxide on the myocardium. The anesthetic agents were administered by means of a pump which maintained the pulmonary ventilation. In any one experimental period the heart did a constant amount of work.

It was found that chloroform caused a rapid dilatation with early rises in the pulmonary and auricular pressures.

Ether caused a marked dilatation of the heart. Beginning at ether blood levels corresponding to second plane anesthesia, the dilatation exceeds the physiologic, as indicated by auricular and pulmonary pressure rises.

Cyclopropane in the anesthetic range causes a dilatation but not so marked as that produced by ether.

Divinyl ether was not studied quantitatively because of the lack of means, but it apparently causes a dilatation greater than that produced by cyclopropane, but not as great as that produced by ether.

Nitrous oxide causes slight cardiac dilatation and this occurs when it is administered with an adequate amount of oxygen.

These effects were the result of the impairment of the efficiency of the myocardium. Pulmonary vasoconstriction with consequent pulmonary hypertension and increased work of the right ventricle was not a cause for increase in the ventricular volume since there was always a considerable degree of dilatation before any rise in pulmonary pressure occurred. Neither was coronary vasodilatation with an increased blood volume a cause for increase in the

ventricular volume since dilatation equal to a third of the initial volume of the heart would be produced and these extreme degrees of dilatation were usually accompanied by a drop in the arterial and, hence, in the coronary pressure.

JACOB T. BRADSHER, JR., M.D.

The Effect of Intravenous Pentothal Sodium, With or Without Inhalation of Oxygen, on Liver Function. C. H. WALTON, J. SALDAMANDO, and W. M. EGNER. *Anesthesiology*, 1951, 12: 67.

Since it has been shown in animals that halogen liver poisoning may be a centrolobular hypoxia secondary to an initial toxic swelling of the parenchyma, it is postulated that a mildly toxic agent, even in the presence of adequate peripheral oxygenation, may produce transient hepatic damage from central hypoxia, which may be aggravated subsequently by low oxygen tensions. Dietary deficiency may predispose to, or even produce, similar parenchymal swelling with a resulting circulatory embarrassment of the liver lobule. In view of the tendency toward respiratory depression following the use of pentothal and the controversial nature of our present knowledge concerning detoxification, it is important to determine the effect of pentothal on the function of the normal and damaged liver of the dog, with particular emphasis on the influence of the inhalation of oxygen.

Previous work in the laboratory of the authors had shown retardation of return to normal function of the chloroform-damaged liver of the dog when pentothal was administered at the height of the dysfunction. However, when the pentothal was given with 100 per cent oxygen the return rate to normal function of the damaged liver was normal. This suggested that pentothal was deleterious because of hypoxemia consequent to respiratory depression and hemodilution, and that correction of the oxygen deficiency eliminated the adverse effect.

The present study is an attempt of the authors to determine whether pentothal per se had any toxic effect on the liver of normal dogs. Pentothal sodium, in doses of 20 mgm. per kilogram of body weight, was given intravenously twice daily to normal dogs for periods of 2 to 3 weeks. Hepatic function, as determined by the prothrombin time and serum bilirubin levels, was mildly depressed with complete return to normal 4 days after the last injection of pentothal sodium. Inhalation of 100 per cent oxygen had no modifying effect on the depression of liver function produced by the employed dosage of pentothal.

It is suggested that in a patient with considerable preoperative liver dysfunction, the administration of pentothal sodium might be a sufficient burden to exceed the limits of tolerance.

JACOB T. BRADSHER, JR., M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Digital Flaps. MICHAEL L. LEWIN. *Plastic & Reconstr. Surg.*, 1951, 7: 46.

Rotation of lateral or laterodorsal skin flaps of the digits over to cover defects on the volar surface of the same digit is an effective way of providing a padded covering over the flexor tendon sheath following the excision of traumatic scar tissue, or Dupuytren's contracture. The donor site is then covered with a full thickness skin graft from the inner arm. This one-stage procedure obviates the multiple stage and the time-consuming procedures necessary when resurfacing is done with brachial or abdominal flaps. Three illustrative cases in which this method was used are reported.

ROBERT L. CRAIG, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

The Inverted Position in Roentgenography. GEORGE V. BUTLER. *Radiology*, 1951, 56: 66.

Roentgenologic examinations are done infrequently by inverting the position of the patient. Thus a cephalad tilting is employed in myelography, and the Trendelenburg position in hysterosalpingography.

The author believes that much additional information could be gained from a wider use of the inverted position in a number of other routine roentgenologic examinations, as, for example, of certain portions of the alimentary and urinary tracts. He, therefore, devised an apparatus which can easily be adapted to any roentgenographic table, thereby greatly simplifying the maneuver of tilting with practically no discomfort to the patient.

The apparatus consists of a special suspension garment, open anteriorly and posteriorly, which at one end is placed around the patient's shoulders and at the other end is fastened to eyebolts in a revolvable circular aluminum plate at the foot of a tilt-type roentgen table. The garment is made of canvas and is provided with buckle-and-strap side combinations for the adjustment of the length of the patient to the table. Other straps may be wound around the ankles and attached to the eyebolts when an inverted position approaching 90 degrees is needed. The circular aluminum plate revolves on an axle which is inserted into the bracket and aligned with the long center axis lying 5 inches above the top of the table. This arrangement permits easy fluoroscopic and roentgenographic examination of inverted patients in anteroposterior, lateral, and any desired oblique projections.

In examination of the alimentary canal, the author found the use of the inverted position increasingly valuable in study of the esophagus, ampulla, gastric cardia, terminal ileum, transverse colon, colonic flexures, sigmoid, and rectum. For this reason, he now has the patient don the suspension garment prior to fluoroscopy and routine roentgenography. The tilting may vary from 35 to 90 degrees, the most suitable position being at 50 degrees below the horizontal. The appearances of the images of the most common lesions of the enumerated portions of the gastrointestinal tract are briefly described.

For the intravenous pyelography also, the patient routinely dons the suspension garment. The first roentgenogram is made in horizontal position prior to the injection of the diodrast, the second and third in 50 degrees inverted position 5 and 15 minutes after injection of the diodrast (the second without, and the third with compression of the lower abdomen), and the fourth roentgenogram in erect position immediately after the third (following removal of the compression). Two advantages are cited by the author as a result of this procedure: (a) the images of the renal pelves and upper ureters are considerably more opaque than in the roentgenograms taken in the horizontal position, and (b) an excellent opportunity is afforded to estimate the range of mobility of the kidneys and ureters, and the ability of the kidneys to empty.

The only contraindications to roentgenologic examination in the inverted position are cardiac decompensation and asthma. The author also proceeds somewhat more cautiously with hypertensive patients, those with heart lesions, the aged, and the obese. Except for some flushing of the face and distention of the superficial vessels of the head, no dyspnea or other untoward effects were noted even when the inverted position was occupied by the patient for 15 to 30 minutes.

In conclusion, it is suggested that the method may also prove of value in examination of the rectum and sigmoid with relatively radiopaque distensible tubes, lipiodol instillation of the upper lobes of the lungs, and in the use of the body weight to produce the vacuum effect in the knee joints.

The article is illustrated with 2 photographs of the apparatus and 13 roentgenograms showing lesions of the esophagus, stomach, and colon, and comparative pyelograms. T. LEUCUTIA, M.D.

Developments in Cerebral Angiography with Rapid Serialized X-ray Exposures on Roll Film 9½ Inches Wide. WENDELL G. SCOTT and WILLIAM B. SEAMAN. *Radiology*, 1951, 56: 15.

Cerebral angiography has become a common diagnostic procedure. In the present article the authors discuss the recent improvements in the quality of the contrast media, in the method of injection and, more especially, in the development of apparatus for the automatic serialization of roentgen-ray exposures. The scope, however, is limited to the injection via the internal carotid arteries, no consideration being given to the injection via the vertebral arteries.

Contrast media. The favored contrast media are: 35 or 50 per cent diodrast, 50 per cent neo-iopax, and 24 to 26 per cent thorotrast. The authors prefer the 35 per cent diodrast because of its lesser irritation to the blood vessels as compared to both the 50 per cent diodrast and the 50 per cent neo-iopax. Thorotrast, although relatively nonirritating, has two disadvantages: (a) it may be sufficiently radioactive to be harmful later in life, especially when injected in children, and (b) it can produce marked local fibrosis in case of extravasation.

Lately the authors used, successfully, 30 per cent urokon on dogs, and are ready to proceed with further investigations on appropriate patients. There can be no doubt that the ideal contrast medium for cerebral angiography is yet to be found.

Method of injection. About 50 per cent of injections are done percutaneously into the common carotid artery with a No. 17 or No. 18 needle. The contrast medium is introduced very rapidly without occlusion of the common carotid artery proximal to the site of injection or of the external carotid. The remaining 50 per cent of injections are given by the open method of exposing the artery in the neck.

The percutaneous approach is considered the more attractive of the two, since, with the use of automatic serialized equipment, it requires only 5 to 7 c.c. of the opaque medium. If, by accident, extravasation occurs, the injection can be repeated two or three times without exceeding the formerly employed quantity of 15 to 30 c.c.

Automatic serialized roentgenographic apparatus. The authors briefly review the salient steps in the development of the mechanization and automatization of the roentgenographic equipment for continuous serialization of cerebral angiography. They then describe in detail their own apparatus (originated by Scott in 1948) which does away with the changing of film cassettes and utilizes a large-size roll film, 9½ inches in width, permitting up to 30 rapid exposures of one-twentieth of a second, at the rate of 2 every second. The first model was presented by Scott and Moore in December, 1948 and was named the "rapidograph." After that the idea was turned over to a camera and instrument corporation, who brought out the factory model called the "roll-film cassette." This model is the one described and illustrated with photographs in the present article.

Since roentgenograms in both the lateral and anteroposterior views are essential for the accurate and complete visualization of the cerebral arterial system, the authors devised the so-called "double rapidograph." In this arrangement two roll-film cassettes are placed at right angles to each other and the exposures in the two views are made simultaneously during and following a single injection of opaque substance. The construction and operation of the double unit is also described at length and illustrated with photographs. In a foot note the authors state that very recently this double unit "has been revamped and simplified in many aspects, largely to provide greater stability and to bring the vertical magazine in closer apposition to the patient's head."

Advantages of serial angiograms. These are listed by the authors as follows: (1) demonstration of the progressive filling of the arterial tree; (2) a definite assurance that the arterial tree will be visualized at its maximum filling; (3) a means of confirming the constancy of a filling defect by comparing a particular film with those taken immediately before or after; (4) elimination of the delay of unloading and loading cassettes; (5) reduction of noise and vibration to a minimum; (6) the possibility of immediately repeating injections, since sufficient film is available on the supply roll.

These advantages are richly illustrated by means of reproductions of excellent serial angiograms.

In concluding, the authors express the opinion that until a completely innocuous contrast medium is found, the continued development of more elaborate equipment, as the double rapidograph, is justified to further reduce the unfavorable reactions associated with cerebral angiography.

T. LEUCUTIA, M.D.

Shortening of the Posterior Wall of the Sella Turcica Caused by Dilatation of the Third Ventricle or Certain Suprasellar Tumors. BERNARD S. EPSTEIN. *Am. J. Roentg.*, 1951, 65: 49.

Changes in the roentgenographic appearance of the sella turcica often indicates the presence of intracranial disease. Such abnormalities are best understood when correlated with pathologic changes coexistent in the brain and its ventricles and the subarachnoid spaces. Shortening of the posterior wall of the sella turcica with or without sellar enlargement or atrophy occurs.

The pathological material upon which this report is based consists of 15 cases of stenosis of the aqueduct of Sylvius, 9 of basilar arachnoiditis, 17 craniopharyngiomas, 30 pituitary adenomas, 18 tumors of the third ventricle, 7 pineal tumors, 10 suprasellar meningiomas, and 7 aneurysms of the internal carotid artery. All were verified either at operation or autopsy with the exception of 5 cases of stenosis of the aqueduct of Sylvius. As controls, the pneumoencephalograms of 35 verified frontal lobe tumors, 55 parietal lobe, temporal lobe, and temporoparietal lobe tumors, and 10 verified intraventricular tumors of the lateral ventricles and corpus callosum were reviewed.

The data reported indicate that shortening of the posterior wall of the sella turcica may occur with or without enlargement and atrophy of the sella. The condition may occur with certain midline lesions which cause pronounced dilatation of the third ventricle. The floor of the third ventricle in such cases may impinge against the posterior wall of the sella turcica and protrude downward into the cisternal interpeduncularis and pontis. Shortening of the posterior sellar wall may also occur when a tumor mass such as a craniopharyngioma or an extrasellar pituitary adenoma impinges against it. In such cases the third ventricle plays no part in the shortening described.

FRANK L. HUSSEY, M.D.

The Transversal Tomogram of the Normal Thorax: a Contribution to the Topographic Anatomy of the Living Man (Das transversale Schichtbild des normalen Thorax, ein Beitrag zur topographischen Anatomie am lebenden Menschen). ALFRED GEBAUER. *Fortschr. Roentgenstrahl.*, 1951, 74: 14.

The author publishes a series of tomograms of the normal thorax in the transversal plane at the levels from the first to the twelfth dorsal vertebrae.

Tomograms of the thorax are usually taken in the vertical plane only and are comparatively easy to interpret by comparison with fluoroscopic and roentgenographic findings. However, no ordinary roent-

genograms can be taken in the transversal plane, and the tomograms taken in this plane show very unusual views which have to be read and interpreted by comparison with cross sections in the anatomic atlas. The heart and the lungs, and the organs of the mediastinum, the diaphragm, liver, and spleen, are visualized as shadows quite different from those we usually see in vertical exposures.

The author suggests division of the pictures into four groups, according to the levels in which they have been taken: diaphragmatic (first lumbar to tenth dorsal), diaphragmatohilar (tenth to eighth dorsal), hilar (eighth to fifth dorsal), and apical (fifth to first dorsal). WERNER M. SOLMITZ, M.D.

Experiences in the Diagnosis of Lung Carcinoma (Erfahrungen bei der Diagnostik des Lungenkrebses). H. ANACKER. *Fortsch. Roentgenstrahl.*, 1951, 74: 2.

As in any other malignancy, early diagnosis is the *conditio sine qua non* to improve the chances of curing lung carcinoma. The author discusses his experiences with different diagnostic methods in a series of 201 cases of suspected cancer of the lung. In 163 of these 201 cases carcinoma was found; in 80 of them the diagnosis was made by biopsy, in 25 by operation only, in 1 by cytologic examination, and in 59 by roentgenography and the clinical course. In 26 cases carcinoma was ruled out, and in 12 the diagnosis remained uncertain. Eighty-eight per cent of the cases were in men, and 12 per cent were in women. The site of predilection was the division of the main bronchus in the upper and lower lobe bronchi.

Of the different diagnostic procedures, the writer considers bronchography as the most valuable. According to his experiences, it is superior to bronchoscopy and tomography. It is contraindicated only in cases of considerable recent hemoptysis and in active tuberculosis. It should always be performed under fluoroscopic control. In cases of central bronchogenic carcinoma it is almost 100 per cent successful. Only peripheral tumors cannot be diagnosed by this method.

According to the American literature (Herbut and others), the cytologic method of Papanicolaou is more reliable and successful than any other single method. The author did not use it because at his institute (X-ray department of the Surgical Hospital at the University of Munich, Germany) no one is sufficiently experienced in the technique of cytologic diagnosis. Differential diagnosis must rule out chronic nonspecific and tuberculous inflammation, bronchiectasis, and benign adenoma of the bronchi.

WERNER M. SOLMITZ, M.D.

High Diverticulum of Stomach (Ueber hochsitzende Magendivertikel). H. R. BECK. *Fortsch. Roentgenstrahl.*, 1951, 74: 47.

The author discusses different types of stomach diverticula, their appearance in the roentgenograph and the signs which permit their differentiation from peptic ulcer.

One congenital form, situated close to the pylorus, originates from aberrant pancreas anlages. This type rarely causes any clinical symptoms.

Another congenital type, the so-called apex diverticulum, is located close to the cardia at the posterior wall of the stomach and may reach the size of a plum. Comparative anatomic studies revealed that it is an anomaly on a phylogenetic basis and is constantly present in the stomach of the hog. It is separated from the rest of the stomach by a circular fold. Also, this diverticulum does not cause clinical symptoms.

A third type is the acquired traction diverticulum caused by adhesions between the stomach and neighboring organs. It occurs after inflammations of the gall bladder or of the pancreas, and after operations.

A fourth type is the functional or pseudodiverticulum caused by local spasms. This indentation of the mucosa can be quite deep; it is shaped like a funnel or a tube and simulates organic diverticula. Only repeated x-ray examinations reveal that it is not constantly present but disappears after relaxation of the spasm.

The author describes a form of diverticulum which he believes to be different from all hitherto known types and which he terms "autoplastic diverticulum." It is located at the posterior fundus wall close to the cardia, has the shape of a niche, and shows marked changes in size and shape in repeated roentgenographs. It occurs in cases of gastritis and is caused by a local atony of the muscularis mucosae accompanied by increased tonicity of the surrounding area. This causes the appearance of a circular wall surrounding the niche. Its differentiation in the roentgenograph from niches caused by peptic ulcer is discussed. Five pertinent cases are reported, and a number of instructive roentgenographs are included in the article. WERNER M. SOLMITZ, M.D.

Relationship of the Nature of the Opaque Medium to Small Intestine Radiographic Pattern. G. M. ARDRAN, J. M. FRENCH, and E. H. MUCKLOW. *Brit. J. Radiol.*, 1950, 23: 697.

Barium sulfate has been employed as a radiopaque medium for many years in the investigation of the intestinal tract. The common vehicles are water or normal saline, with or without suspending agents such as gums.

Seven patients in whom a flocculated pattern of the small intestine had been observed, during routine radiography with simple suspensions of barium sulfate, were selected for study with a thixotropic gelocolloid preparation of barium sulfate (raybar) which does not flocculate in vitro with freshly secreted mucus.

In normal subjects, examination of the pattern of the small intestine with two types of meal showed no essential difference. The normal feathery mucosal pattern was seen with "raybar." In abnormal subjects there was a marked difference in the pattern of the small intestine between the two types of meal. With the simple suspensions the pattern was

of the clumped or "deficiency" types, significant segmentation having occurred in the small intestine with absence of the normal feathery markings, obliteration of the valvulae conniventes, and smoothing of the margins of the barium outline. With "raybar" suspension, segmentation did not occur. The contrast medium was seen in continuous columns, with clear markings of the valvulae conniventes, in a dilated small intestine.

The authors conclude that meals of simple and complex suspensions of barium give different radiographic patterns in the small intestine in certain cases, and that the difference in pattern may be largely attributable to the method of suspension, and not to changes in the clinical state of the patient.

FRANK L. HUSSEY, M.D.

Lymphatic Pseudopolyposis of the Ileum—Pseudoileitis (Pseudopolyposis lymphatica ilei—pseudoileitis). J. BUECKER and H. R. FEINDT. *Fortsch. Roentgenstrahl.*, 1951, 74: 59.

Several writers (R. Golden and von Stroembeck) described a nonsclerosing ileitis which they considered as a special type of regional enteritis.

The author reports 5 cases in children and young adults in whom x-ray revealed polypoid excrescences and irregularities in the contour of the terminal loop of the ileum. These findings were observed partly with and partly without a clinical history of enteritis. The cobblestone appearance of the intestinal mucosa was evidently caused by hyperplastic lymph follicles. In 1 case this could be confirmed by biopsy; the mucosa was found to be normal in this instance.

The writer believes that the afore-mentioned x-ray findings do not necessarily indicate disease of the intestine, but may be present in normal individuals with a tendency toward hyperplasia of the lymph follicles. In some of his cases, enlargement of the regional lymph nodes was present also in other areas of the body.

WERNER M. SOLMITZ, M.D.

Cysts of the Kidney. HAROLD C. OCHSNER. *Am. J. Roentg.*, 1951, 65: 185.

The author reviews the cases of renal cysts for the years 1944 to 1948, inclusive, diagnosed at the Methodist Hospital, Indianapolis. During this period 107,656 in-patients were admitted to the Hospital and 8,948 cystoscopies were performed. Simple cysts of the kidney are found more frequently in the lower pole. The next most common site is the upper pole, while cysts are least likely to be found in the central portion of the kidney. Neither kidney seems to be favored. Many complications of simple cysts of the kidney have been observed. There is frequently concomitant urinary tract infection. Calculi are occasionally encountered, either large simple, or calycine cysts. Pyelographic abnormalities in the presence of cysts include changes in the contour and size of the calyces and renal pelvis, and disturbances in the position and outline of the ureter.

The symptoms of the patients who had either surgical or clinical evidence of large simple cysts were quite variable. One patient had noticed an abdominal tumor; 1 had a dragging sensation in the flank; 1 had hematuria; and 1 had pain in the back and flank. One patient with prostatic hypertrophy had straining, urgency, and frequency, but no symptoms referable to the renal cyst. One of the 2 patients who had calycine cysts with associated calculi complained of stone colic, but the other had no local symptoms. There were 9 surgically proved and clinically accepted simple serous cysts of the kidney, 2.5 cm. in diameter or over. The calycine cysts were 4 in number. Hemorrhagic cysts of the kidney are not encountered so frequently as simple cysts; only 1 case was encountered in this period. There was hematuria and a mass in the kidney region in this case. In this series there were 3 patients with multilocular cyst of the kidney; only 1 of these had symptoms directly referable to the kidney. The pyelographic findings in these 3 cases resembled those found in hypernephroma. There were 25 patients with polycystic disease in this period. The most common complaints of the patients of this group were hematuria and abdominal pain. Three of the patients complained of frequency and 5 complained of the presence of an abdominal mass.

The roentgenographic findings in polycystic disease are quite distinctive. The calyces and pelvis of each kidney are usually dilated, elongated, and greatly distorted; they have a sprawled out appearance; and the minor calyces are often crescentic. The kidney outlines are often indistinct in the preliminary film and, when visualized, are very large. The involvement is almost always bilateral. Fifteen patients among 897 postmortem examinations were found to have simple serous cysts. Two cases of polycystic disease of the kidneys were found. A simple classification of renal cysts is given:

I. Congenital Cysts
  A. Polycystic disease of the kidneys
    1. Unilateral
    2. Bilateral
II. Acquired Cysts
  A. Simple serous
    1. Large "solitary"—may be multiple
      a. No connection with pelvis or calyces
      b. Pyelogenic
    2. Calycine
  B. Hemorrhagic
    1. Spontaneous
    2. Traumatic
    3. With malignant disease
  C. Multilocular
  D. Retention (small cysts of chronic sclerosing renal disease)
  E. Secondary to other renal pathological changes
    1. Infectious
    2. Neoplastic

FRANK L. HUSSEY, M.D.

Generalized Hyperostosis and Similar Systemic Diseases of the Bones (Die generalisierte Hyperostose und aehnliche Systemerkrankungen der Knochen). ALFRED VOGT. *Fortsch. Roentgenstrahl.*, 1950, 73, 411.

The author describes a case each of four types of generalized hyperostosis: (1) the typical completely developed type in the juvenile patient, which advances symmetrically and by successive attacks, (2) the symmetrical type which advances by attacks in the adult, (3) the asymmetrical type with preponderantly endosteal osteosclerosis in the adult, which advances by attacks, and (4) the generalized type with preponderant participation of the compact bone and polyostotic localization, but incomplete symmetry.

The comparison of the roentgen findings in the bone system of the first patient with those of the other 3, in whom the lesions were largely similar but did not involve all of the bones, nor reach the marrow and the periosteum in the individual bones, permits a discussion of the concept of generalized osteosclerosis, with reference to its extension to the marrow and the periosteum. Only surmises can be advanced concerning the type of disease in the last 3 cases. There is undoubtedly a true systemic disease of the bones. The similarity of the individual roentgen pictures with those of typical generalized osteosclerosis makes it probable that the changes which can be demonstrated roentgenologically are the expression of functionally conditioned end structures in still obscure insidious diseases of the bone building cells. In 1 of the patients an acute stage could be observed, while in another the bone disease progressed insidiously and chronically under the clinical picture of a rheumatic disorder with lumbago and sciaticalike disturbances. In the third patient an acute stage could not be remembered.

Vogt thinks that these patients present, etiologically, very different diseases which have in common the similarity of the roentgen picture and the fact that the common factor, which is more obvious in one case than in another, is generalized osteosclerosis involving the inner space of the bone and the periosteum. It must be noted that these bone disorders all have a chronic course and develop very slowly, like Paget's disease; their progression may extend over decades and even during the entire life of the patient. This is the reason why so little is still known about the forms of generalized hyperostosis. Such forms are often erroneously taken for atypical Paget's disease. Only roentgen criteria can be considered for the differential diagnosis, since the clinical phenomena of the disorders included in the concept of generalized hyperostosis are so indefinite as not to raise any suspicion of the true condition which is present.

As to the mineral metabolism, Vogt regrets not to be able to give any information because during and after the war pertinent laboratory studies were out of the question in Tuebingen. However, it was observed that during the acute attacks there was a strong increase in the sedimentation rate of the red blood cells and a slight secondary anemia.

RICHARD KEMEL, M.D.

A Roentgen Study of Skeletal and Intrathoracic Metastases from Salivary Gland Cancer. DANIEL WILNER. *Radiology*, 1950, 55: 801.

The author presents a report of 49 histologically proved cancers of the major salivary glands with metastases to the chest or to the skeleton, as revealed roentgenographically.

Salivary gland metastases to bone produced three types of lesions: (1) erosive, (2) patchy, and (3) lytic.

Thirty-three cases showed metastasis to bone. In 21 of these the metastasis was of the solitary form and in 12 there were metastases to 2 or more bones. The location in the skeleton was as follows: mandible, 20; spine, 8; pelvis, 6; skull, 5; ribs, 3; femur, 3; scapula 1; and humerus, 1. A soft tissue mass was observed in only 3 cases.

The metastases to the lungs were of two forms: (a) nodular, and (b) miliary. There were 23 cases of pulmonary metastases. One patient with deposits within the chest had mediastinal involvement, while 7 patients with pleural reaction had pleural metastases.

FRANK L. HUSSEY, M.D.

Roentgen Diagnosis and Treatment of Osteoclastoma; Benign Solitary Giant Cell Tumor of Bone (Die Roentgendiagnostik und Strahlentherapie des Osteoklastoms, gutartiger solitaerer Riesenzelltumor der Knochen). E. MIGNOLI and U. COCCHI. *Fortsch. Roentgenstrahl.*, 1950, 73: 391.

During the past 30 years, from 1920 to 1949, inclusive, 50 patients with osteoclastoma were admitted to the Roentgen Institute of the University of Zurich; 40 were between the ages of 11 and 50, and 58 per cent were females. The diagnosis is very difficult in the beginning of the disease because the cases are rather infrequent and often show no clinical symptoms. There may be rheumatic pains, slight swelling of the involved site, and a good general condition, and the tumor can be detected only by roentgen examination associated with biopsy. Traumatism was mentioned in 9 of the 50 histories.

Roentgenologically, there is a central and a cortical form of osteoclastoma. The initial stage is characterized by a small round or oval, sharply delimited clearing lying in the bony tissue and resembling a cyst. In the central form the disease is located in the epiphysis, seldom in the metaphysis. In the course of further development of the tumor, the bone increases in size and looks as if it were inflated from inside; the normal spongiosa structure largely disappears, leaving heavy cords between which there are clearings resembling a honeycomb and acquiring the aspect of a mass of large soap bubbles. Important for the diagnosis is the prolonged intactness of the cortex which shows as a thin, sometimes veil-like shell, without signs of periosteal reaction. The involved bone remains well

delimited from the articular cartilage. As the disease progresses, the soap bubble picture changes to one of pure osteolysis, the member becomes greatly swollen, and its function is reduced. Finally, the cortical layer also disappears, leaving a large bone defect. In the cortical form (borderline cases according to Ewing) the disease occurs in the metaphysis and diaphysis of the long bones, especially in the fingers, and the picture is one of circumscribed, bowl-shaped, subperiosteal bone defect. The development of osteoclastoma from its onset to the full-blown stage may be very slow and takes from a few weeks to 2 years; clinically, it may be completely silent. In this case, the tumor is sometimes revealed by a spontaneous or traumatic fracture; there were 4 spontaneous fractures among the 50 cases. If the tumor is untreated, malignant degeneration into sarcoma or fibrosarcoma may occur, but this is denied by many authors. The sites of predilection of the tumor are the distal epiphysis of the femur, the proximal epiphysis of the tibia, and the distal epiphysis of the radius.

Usually, the prognosis is rather good and treatment leads to complete healing, but there are occasional recurrences. There were 5 patients with malignant degeneration; 2 were cured by amputation and 3 died of pulmonary metastasis. Treatment may be surgical, roentgenologic, or a combination of the two. Of the 50 patients with 51 tumors, 23 were treated by irradiation; 20 (87 per cent) were cured and 3 were not, but 1 of the latter underwent amputation and has been symptom-free for 14 years. The 2 others developed malignant degeneration of the tumor; 1 of them died and the other had an amputation. Five patients were treated surgically: 3 were cured but 1 of them has disappeared; 2 patients had a recurrence and were operated upon again and then disappeared. Of 23 patients submitted to combined treatment, 21 (91 per cent) were cured; the other 2 developed malignant degeneration of the tumor and died. Altogether, cure was obtained in 84 per cent of the patients. After 5 years 70 per cent remained cured; there were 6 recurrences (12 per cent).

Irradiation consisted of single doses of from 150 to 200 roentgens, the total dose varying from 2,000 to 13,500 roentgens. The duration of the treatment ranged from 20 to 50 days. This treatment was well tolerated and no serious side effects were observed. It is the treatment of choice in all cases that are not too far advanced. RICHARD KEMEL, M.D.

The Significance of Roentgen Diagnosis for the Operative Treatment of Intervertebral Disc Prolapse (Die Bedeutung der Roentgendiagnostik für die operative Behandlung des Bandscheiben-Prolapses). ARNOLD HOFMANN. *Fortsch. Roentgenstrahl.*, 1950, 73: 442.

On the basis of more than 350 operations performed since 1938, the author distinguishes between true nucleus pulposus prolapse and disc prolapse in which a large part of the hard annulus fibrosus is also involved. In addition, he divides both groups into temporary, complete, and calcified forms, the latter being particularly serious when they occur in the cervical and thoracic regions. Prolapse in the lower cervical and in the thoracic region is rare, while that in the lumbar region amounts to from 90 to 95 per cent of the cases.

The characteristic history is of the greatest value for the diagnosis, but many patients do not have such a history and a careful neurologic examination is necessary to decide the question. Roentgen examination, particularly myelography and generally with iodipin (at most 2 c.c. of 20 per cent concentration), has been used by Hofmann very often since the end of 1947, and the films were nearly always unequivocal, while subsequent pain was reduced to a minimum. The so-called waist and wristlet phenomena may lead to error and be confused with lateral protrusion or protrusion occupying the entire width of the vertebral canal; they can probably be explained by osseous or ligamental narrowing. A negative myelogram does not mean that there is no prolapse. Hofmann has operated upon many patients of whom the film was negative or only suspicious, and found a prolapse. Special attention should be paid to compression of nerve elements by spondylitic border swellings, ossifications, and calcifications, and exposures must be taken in various positions in these cases.

Peridurography or epidurography after the epidural space was filled with 30 per cent viscous perabrodil revealed that not too much reliance can be placed on this method. Air myelography may give very good films, but in general is not reliable enough in view of the great number of prolapses in the region of the two lower discs where the conditions for clear lateral films are bad. Lately, the use of abrodil for high exposures has again come into use: the exposures must be made immediately after the injection to obtain as much contrast as possible because the substance is rapidly absorbed. From his experience with about 50 cases, Hofmann believes that the sagittal exposure, which gives the best results with iodipin, is not as valuable as the lateral and oblique exposures. Especially with the latter, the feathered relief of the elements of the cauda is demonstrated.

Except for attacks of cramps in 1 patient, the side effects of the method were so slight and of such short duration as to be incomparable with those resulting from the use of iodized oil. RICHARD KEMEL, M.D.

Roentgenologically Demonstrable Soft Tissue Changes in the Knee Joint Region and Their Significance (Roentgenologisch nachweisbare Weichteilveraenderungen im Kniegelenksbereich und ihre Deutung). MARTIN MEIER-SIEM. *Fortsch. Roentgenstrahl.*, 1950, 73: 479.

The soft tissues of the knee joint visible in the roentgenogram depend on the age of the patient. Thus, in the small child the fatty layer shows up distinctly and cartilage may occasionally be recognized; in adults the muscle and tendon portions are

more strongly defined and the fatty layer over the femoral metaphysis becomes thinner; in older subjects with arteriosclerosis, calcification of the muscle and tendon attachments is frequently observed; and with the physiologic decrease of the cartilaginous layer the articular cleft becomes narrower.

In prepatellar bursitis there is a homogeneous shadow between the subcutis and the patella. In acute inflammatory processes the subcutis, which normally is narrow, is decidedly wider and shows a netlike formation as an expression of the edema; the capsular region is unchanged.

Thickenings of the capsule jeopardize the differentiation of the soft tissue picture. The plica alaris becomes indistinct and the capsule itself in the region of the upper recess may become recognizable as a linear thickening.

Knee joint effusions are nearly always demonstrable roentgenologically if the appropriate technique is used. Increase in the effusion leads first to filling of the upper recess. This recess often communicates with the suprapatellar bursa and then reaches up to the femoral metaphysis. In such cases there is a homogeneous shadow in the region of the upper recess, delimited like an arc. The tendon picture disappears and the zone of clearing over the femur becomes narrow and may disappear altogether. Only with marked effusion is the patella displaced forward, and then only when the femoral extension muscles are relaxed because the patellar ligament does not stretch. The increased joint fluid fills also the posterior recess which then protrudes bilaterally to the greatest extent. The bands which enclose the knee joint vary in tension, according to the position of the joint; this also changes the filling of the recess. The upper recess fills more when the leg is extended; the posterior recess fills more when the leg is flexed. When effusion is suspected, the shadow should also be searched for posteriorly. RICHARD KEMEL, M.D.

MISCELLANEOUS

Problems of Clinical Radiobiology. JORGEN E. THYGESEN. *Radiology*, 1951, 56: 403.

The author discusses the need of a physiological and biological approach to the field of radiation therapy. This view is particularly important in the radiation of large volumes of tissues in which the therapist must take cognizance of the stress on the irradiated biological organism as a whole. The physical dose or energy of the total radiation absorbed can be measured by the integral dose of Mayneord. However, the biological dose problem is more difficult to assess. Consequently, the author urges the transference of the radiobiological experiment to the radiation therapy clinic so that adequate studies may be made.

In order to approach these problems, the author has adopted a homeostatic concept. This pertains to the ability of the organism as a whole to maintain certain physiological constants in the face of changing external conditions or stress factors. Since the final results of severe stress include the impairment of cellular function, an individual radiation tolerance of man may probably be expressed by his capacity for homeostatic regulation of oxygen transport. Since the ultimate results of stress are anoxia, the capacity to maintain regulation of the oxygen transport may be threatened by anemias, an increased basal metabolism rate, malnutrition, and dehydration.

The author discusses some of the methods which may be used to measure the biological effects on the irradiated patient and his ability to withstand treatment. These methods include total blood volume determinations before, during, and after irradiation, and total hemoglobin determinations. Sjöstrand's carbon monoxide method for determining the blood volume was found to be rapid and exact.

MAURICE D. SACHS, M.D.

The Diagnosis and Treatment of Radiation Sickness in Atomic Warfare. EUGENE P. CRONKITE. *West. J. Surg.*, 1951, 59: 55.

The injuries occurring after an atomic bomb attack are due to the blast, the thermal effect, and radiation exposure produced by the explosion. In the period immediately following the explosion the burden of diagnosis and the treatment of these injuries will fall on all surviving physicians within the bombed area. After the initial shock has subsided, however, it will be found more expedient to segregate the various types of casualties and send them to (1) traumatic centers, (2) burn centers, and (3) radiation treatment centers, where they are placed under the care of competent specialists.

In the present article the author deals only with the diagnosis and treatment of radiation injury uncomplicated by trauma or thermal burns. This type of injury may be subdivided into (a) radiation burn due to beta activity of fission products, and (b) total body irradiation or "the syndrome of acute radiation injury" due to the effect of the gamma rays and neutrons. When the bomb explodes close to the ground, or underneath the surface of the water, considerable beta activity may be present leading to superficial radiation burns, but when the detonation occurs high in the air the whole body is exposed to penetrating irradiation resulting in acute radiation injury.

The author distinguishes between 5 phases of the burns produced by beta activity:

1. Itching, burning, and tingling appearing almost immediately and followed within a few hours by hyperemia and slight edema; this phase lasts 2 or 3 days and subsides almost completely.

2. An asymptomatic period of 3 to 7 days.

3. Secondary erythema returning within 5 to 12 days and reaching a bullous stage with consecutive desquamation within 2 to 4 weeks after exposure.

4. Recrudescence of the signs and symptoms manifested in the third phase, accompanied by deeper necrosis and excessive pain.

5. The chronic phase begins about 3 months after exposure and lasts through lifetime, the late sequelae

consisting of telangiectasia, hyperkeratoses, atrophic ulcers and cancerous degeneration. The treatment of the beta radiation burns is similar to that of the thermal burns, except that a lifetime follow-up is necessary to detect the possible occurrence of late sequelae.

The casualties resulting from total body irradiation or the syndrome of acute radiation injury are divided into 3 groups: (1) improbable survivals consisting of bed patients unable to care for themselves, who are given palliative care, (2) possible survivals consisting of partial bed patients, at times unable to care for themselves, requiring active therapy and prolonged hospital care; (3) probable survivals requiring first aid and reassurance, able to care for selves, who return to civilian duties, and who are observed intermittently; a few will become hospital patients. The author includes a table giving a 3-scale priority system for the transportation and treatment of the casualties in the 3 groups, by subdividing the type of casualties into uncomplicated radiation injuries, complicated radiation injuries (burns and trauma), and no radiation injuries, but burns and wounds only.

LeRoy listed the signs and symptoms of the acute radiation syndrome observed in the Japanese casualties as follows:

Specific signs such as (1) epilation and (2) purpura; suggestive symptoms such as (1) vomiting on the day of exposure, (2) oropharyngeal lesions occurring 39 days after exposure, with pain, ulceration, necrosis, and gingivitis; (3) hemorrhagic manifestations other than purpura. To the specific signs one can add lymphopenia detectable within 24 hours if the casualty was in the lethal zone.

The most valuable symptom, from the point of view of segregation, is vomiting on the day of the bombing. Utilizing this, and the subsequent clinical behavior as a basis, the author gives a detailed account of triage of the exposed population into the aforementioned three groups.

The therapeutic procedures vary considerably in the three groups. In general, they follow established principles which are discussed by the author at considerable length. The opinion is expressed that modern western medicine with adequate supplies of fresh blood, stored plasma, antibiotics, sterile parenteral fluids, and sterile dressings can do much toward alleviation of suffering and toward the increase of survival rates.

In conclusion, the author stresses the point that a standardized treatment is necessary and that medical care, to be effective, must be organized on a state, regional, and national basis. T. Leucutia, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Effects on Human Subjects of Intravenous Fat Emulsions of High Caloric Potency. B. G. P. Shafiroff and John H. Mulholland. *Ann. Surg.*, 1951, 133: 145.

The metabolic effects of single intravenous infusions of one liter of 10 per cent, 15 per cent, and 20 per cent combined fat emulsions were studied in a series of human subjects. The caloric value of a liter of the 10 per cent combined emulsion was 1,289 calories, that of the 20 per cent emulsion was 2,102 calories.

For the attainment of high caloric potency and maximal utilization, it was administered intravenously in the following manner: 500 ml. of the emulsion, 1,000 ml. of 10 per cent glucose in water, and 500 ml. of the emulsion. Clinically, the 10 per cent emulsion gave the least reaction and was best tolerated. The rate of disappearance of fat from the blood was determined by serial chylomicra counts. Oxygen consumption increased during the period of fat intake. There was no fat spillage in the urine.

Repeated infusions of the combined fat emulsion were administered daily in a series of 8 surgical patients. The minimal daily caloric supply averaged 1,689 calories. The maximal intravenous fluid volume did not exceed 2 liters. One patient with a cervical mediastinotomy received infusions for 11 consecutive days. Clinical studies failed to reveal evidence of hemolytic anemia, lipoid pneumonitis, or liver or kidney toxicity. Surgical biopsy examinations were negative for fatty degenerative processes. Weight gain and restoration of nitrogen balance were noted. B. G. P. Shafiroff, M.D.

Congenital Anomalies of the Hand. Arthur Joseph Barsky. *J. Bone Surg.*, 1951, 33-A: 35.

At the present time the most accepted theories of congenital malformations are those of maldevelopment or of mutations which are subsequently inherited.

Syndactylism appears to be the most common congenital deformity of the hand. It is observed most frequently between the middle and ring fingers, and between the second and third toes. Syndactylism is often associated with polydactylism. There are two main types of operative procedure—(1) flap operation and (2) a free skin graft, or a combination of the two may be used.

Polydactylism is a part of the general phenomenon of duplication of parts. It tends to be inherited, and is often associated with other congenital anomalies. There is a tendency for the condition to be marginal, rather than centrally located. The usual form is hexadactylism. There are three main types: (1) just an extra fleshy mass, (2) duplication of the digit, and (3) an extra digit with its own metacarpal or metatarsal bone (quite rare).

Brachydactylism was the first example of Mendelian inheritance demonstrated in man. In this condition, one or even all of the digits are shortened. In some cases the profundus tendon is attached to the distal phalanx and the finger tip can be flexed—in others this is not so.

Annular grooves may be simply shallow grooves in the skin or subcutaneous tissue involving only one digit, or there may be multiple deep grooves extending down almost to the bone with a small distal segment of the finger attached by a pedicle. It may occur in the leg, foot, or the fingers. Operation consists of excision of the grooves, the operation being done in two stages, one-half of the groove excised at each stage. Complete absence of digits or of hands also occurs. It is probably due to genetic determinants rather than to intrauterine amputations.

Cleft hand is a rare congenital anomaly in which there is a defect of the central portion of the hand, and the remaining digits are divided into a radial and an ulnar group. There are several varieties of this so called lobster-claw hand, and treatment varies with the individual case.

Congenital absence of the radius in part or whole is fairly common, and is generally associated with club hand. Another rare anomaly is hypertrophy of the digits, called megalodactylism. The second and third digits are most likely to be involved.

Ely Elliott Lazarus, M.D.

Teratoma of the Sacrococcygeal Region. (Il teratoma della regione sacro-coccigea). Luigi Piacentini. *Arch. ital. chir.*, 1950, 73: 295.

The case of a 4 month old female child with a teratoma of the sacrococcygeal region is reported. The tumor conformed to the classification of bidermoma.

A review of the literature indicates a symptomatology which varies with the site of the lesion. The prognosis should be guarded because of the occasional appearance of a malignant tumor in association with the teratoma. Radical surgical removal is indicated. Edith B. Farnsworth, M.D.

Cutaneous Cancer in Chronic Endemic Regional Arsenicalism in the Province of Cordoba, Argentine Republic (Los canceres cutaneos en el arsenicismo cronico regional endemico en la provincia de Cordoba, R. A.). Ramón A. Argüello, Enrique E. Tello, Berardo A. Mácola, and Lucio Manzano. *Rev. Fac. cienc. méd. Univ. Córdoba*, 1950, 8: 409.

The well water of eastern and southeastern portions of the province of Cordoba, especially in the country districts, is frequently high in arsenical content. It is from the country districts that the major-

ity of cases of arsenicalism come. Here the problem of wholesome drinking water, except for some construction of rainwater cisterns, is entirely unsolved. Of 323 cutaneous cancers received at the University service in Cordoba during the years from 1932 to September, 1939, 39 (12 per cent) presented evident symptoms of chronic, endemic arsenical intoxication; among a further 169 cases observed during 1939, there were 26 instances of arsenicalism (13 per cent). Since this time the percentages have remained about the same. The authors are now reporting 90 cases of associated chronic arsenical intoxication and skin cancer observed during the period from 1932 to October 15, 1949.

The capital and unequivocal symptoms of arsenical intoxication in these patients have been the palmar and plantar digital keratodermias, with or without hyperhydrosis, melanodermia, or leucomelanodermia. These manifestations are at times associated with warty excrescences (keratomas) of the dorsum of the hands, onychia, alopecias, some dryness of the skin, or seborrhea with dirty-looking crusts, resembling the senile keratoma. The arsenical keratoma is dry, rough, and hard. These changes frequently start as reddish patches with a mild grade of desquamative changes or as papules.

In the 90 cases of epithelioma now reported, and the 65 cases previously reported, the localization has been on the extremities (upper limbs, 45; lower limbs, 16) most frequently, the neoplasm usually being single and of the spinocellular type. The usual neoplasm on the trunk has been in the form of Bowen's disease (9 cases); there were 4 instances of true Bowen's disease, 2 instances of Bowen's disease with spinocellular carcinoma, and 3 instances of Bowen's disease with basocellular carcinoma, or of multiple, superficial epitheliomatosis. The patients in the last group presented as many as 100 epitheliomatous lesions, often with the history of a lengthy period of evolution. JOHN W. BRENNAN, M.D.

EXPERIMENTAL SURGERY

The Influence of Cortisone on Skin and Wound Healing in Experimental Animals. HAMILTON BAXTER, CARL SCHILLER, JOHN WHITESIDE, and RICHARD E. STRAITH. *Plastic & Reconstr. Surg.*, 1951, 7: 24.

It has been shown in the rabbit that ACTH or cortisone retards the growth of all elements of the connective tissue, and the growth of granulation tissue in open wounds as well as that about fractures. The same inhibitory effect on wound healing has also been shown to occur in the mouse, and finally, thinning of the epidermis and atrophic changes in the sebaceous glands and panniculus adiposus have been demonstrated in the rat after the parenteral injection of ACTH.

From the results of the studies performed by the author, it is believed that parenterally administered cortisone inhibits the growth of granulation tissue. The significant change was a quantitative decrease in proliferating fibroblasts and capillaries. In addition, this was reflected in the delay in the filling in of the wound space and the development of firm union of the wound edges. This lack of firm union may be due to a deficiency of the epithelium or lack of support by granulation tissue.

It appears evident that one of the many actions of cortisone is to inhibit inflammatory reaction and to reduce excessive fibroblastic proliferation. This hormone probably causes changes in the connective tissue cells so that they no longer react to their usual stimuli. This effect may possibly be due to an alteration in cell permeability.

ORVILLE F. GRIMES, M.D.

The Influence of ACTH on Wound Healing in Man. HAMILTON BAXTER, CARL SCHILLER, and JOHN M. WHITESIDE. *Plastic & Reconstr. Surg.*, 1951, 7: 85.

The authors studied the effect of doses of around 100 mgm. of ACTH daily, for periods up to 2 weeks, on wound healing, epithelization of donor areas, autograft, homograft survival, and on skin.

The rate of healing of incised wounds of skin in man may or may not be delayed by ACTH under these circumstances. In those cases in which a delay of healing occurred the pattern of healing of the wounds was unaltered. The variation in rate of wound healing may be due either to a variation in adrenal response, or in reaction of the tissues to the same amount of adrenal hormone.

The survival of a homograft was not prolonged by 100 mgm. of ACTH therapy daily for 2 weeks. The normal rate of healing of an autograft was not delayed. Epithelization of donor areas was not retarded. Atrophic changes of the skin or its appendages were not found.

Parenteral administration of ACTH is sometimes accompanied by serious side effects which demand careful clinical and laboratory supervision of each case. SAMUEL KAHN, M.D.

The Behavior of Autogenous Human Tissue Grafts. LYNDON A. PEER and JOHN C. WALKER. *Plastic & Reconstr. Surg.*, 1951, 7: 73.

Free, autogenous human grafts were studied under two conditions of transfer: in contact with unlike tissues and in contact with like tissues.

The cells in cartilage, septal bone, fascia, tendon, and surface skin grafts all tend to survive, the tissues retaining their specific structure. Thus, cartilage appears as cartilage, fascia as fascia, regardless of whether the recipient site consists of like or unlike tissue. There is no evidence of mass replacement of the graft cells by infiltrating elements from the host tissues.

Rib, tibial, and iliac bone grafts, in contact with unlike tissues, are replaced by host fibrous tissue, regardless of the thickness or thinness of the grafts or the vascularity of the host site. The bone cells in the grafts often survive transplantation but they are unable to maintain their calcified intercellular material, which is absorbed and replaced by host fibrous tissue

in a period of about 8 months. Rib, tibial, and iliac bone grafts in contact with bone tend to retain their calcified structure.

About 50 per cent of the fat cells in fat grafts survive transplantation, and these surviving fat cells, together with their connective tissue framework, comprise the bulk of the fat graft which remains 1 year or more following transplantation. There is no evidence that cellular elements from the host tissues take on fat and replace fat cells in the graft. Fat grafts transplanted in contact with fat have the same fate as fat grafts transplanted in contact with unlike tissue.

The muscle cells or fibers in free muscle grafts always degenerate and disappear following free transplantation, irrespective of whether the graft is in contact with unlike tissues or with muscle. The fibroblasts in the connective tissue framework of muscle grafts survive transplantation; these cells, together with infiltrating host fibroblasts, convert the muscle graft into a small fibrous tissue band in about a month.

The epidermis, hair follicles, and glands tend to degenerate and disappear in buried skin grafts and dermal grafts. The fibroblast cells in the dermis survive transplantation, associated with the bundles of collagenous and elastic fibres, which constitute the bulky intercellular portion of the dermis. Buried skin grafts and dermal grafts are all in contact with unlike tissues.

When nerve grafts are transplanted in contact with unlike tissues, the fibroblast cells in the framework of the graft survive and proliferate to such an extent that they completely replace the degenerating axons and myelin sheaths. The Schwann cells survive the initial shock of transplantation, but they disappear among the large number of proliferating fibroblasts. When nerve grafts are transplanted in accurate contact with nerve the Schwann cells survive, but the axons and myelin sheaths degenerate and disappear. A few axons from the proximal host nerve grow down through unobstructed channels in the nerve graft and continue on into the distal end of the host nerve.

When the cells in the grafts were killed by alcohol or heat before transplantation, and the grafts were in contact with unlike tissues, all were replaced by fibrous tissue or mixed connective tissue derivatives. None of these grafts was replaced as the same type of tissue by the surrounding host cells. When dead grafts were transplanted in contact with like tissue, the grafts were also replaced by connective tissue, excepting bone in contact with bone and nerve in accurate contact with nerve. Bone and nerve tend to be replaced as the same type of tissue by infiltrating cells from the host bone and nerve.

Roux's law of functional stimulation is important for the survival of highly specialized tissues such as bone, muscle, the glands, and hair follicles in skin.

Tissue fluid exuding from the host site prevents desiccation of graft cells, but this is not an important factor in providing nourishment and oxygen to the centrally located cells, which are remote from this surface fluid. Experimental work has demonstrated that the cells in skin grafts will remain alive for 4 days at body temperature if the grafts are merely stored in a humid atmosphere.

The vascular system in free grafts tends to survive transplantation, and early circulating blood for these surviving blood vessels of the graft is provided through direct anastomoses of host and graft blood vessels. If this blood reaches the centrally located cells in 4 days, the cells may not die from the effect of their accumulated waste products and lack of oxygen.

A cell survival theory applying to all of the grafts in this experimental work may be postulated as follows:

"The cells in free autogenous human grafts tend to survive following transplantation when they are transplanted as complete cell entities in favorable transplantation sites." SAMUEL KAHN, M.D.